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THE PROBLEM OF LOCALIZATION IN EXPERIMENTALLY INDUCED CONVULSIONS*

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The question of the site of origin of the clonic and the tonic elements of convulsive seizures has been much debated. Much experimental and clinical evidence has been adduced to support the contention that the cortex is the source of the clonic and that subcortical mechanisms are responsible for the tonic parts of the motor disturbances, but it has been demonstrated experimentally by a number of investigators, including ourselves,[1] that clonic convulsions can be produced in animals after the total excision of the cortical motor areas of both sides of the brain.

In this paper we shall limit ourselves to a consideration of some features of this problem and shall attempt to give a solution that is based on a large series of experiments on animals, which have led us to apply to the question the ideas of Hughlings Jackson [2] on the change in the quantity of nervous energy which may flow through a given mechanism, pathway or level. To this we have added some remarks on the functional changes that have occurred during the evolution of

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* Read at a Meeting of the Association for Research in Nervous and Mental Disease, New York, Dec. 27, 1929. This paper is based, in part, on a report read by Dr. Pike at a Meeting of the Section on Convulsive Disorders of the American Psychiatry Association, Atlanta, Ga., in May, 1929 (Am. J. Psychiat. **9**:259, 1929), and in part on new experiments.

1. Pike, F. H., and Elsberg, C. A.: The Occurrence of Clonic Convulsive Seizures in Animals Deprived of the Cerebral Motor Cortex, Am. J. Physiol. **72**:337, 1925.

2. Jackson, Hughlings, cited by Horsley, Victor: Dr. Hughlings Jackson's Views of the Function of the Cerebellum as Illustrated by Recent Research, Brit. M. J. **1**:803 (April-June) 1907.

the central nervous system, views which have already been expressed, among others, by Steiner,[3] von Monakow,[4] Orton[5] and one of us (F. H. P.[6]).

The determination of the location of cells or cell groups in which the impulses which lead to motor manifestations originate, and of the fiber tracts through which these impulses are transmitted to muscles, has a bearing on many questions connected with convulsions, not only in the symptom complex commonly called "epilepsy," but also in the convulsions that occur with tumors and other expanding lesions within the cranial cavity, with cerebral arteriosclerosis and other vascular lesions, after trauma to the skull and even in uremia and eclampsia, in asphyxia and perhaps in ordinary syncope. Such studies may throw light on the larger question of the functional organization of the central nervous system as a whole for the initiation and control of normal biologically adequate movements of all kinds. At present there is no generally accepted view of the organization of the general motor system, and this is reflected in the diverse and conflicting beliefs regarding the site of origin of epileptic and other convulsions.

The problem of localization is of interest and importance from the point of view of the pathogenesis of the convulsive states. If one can gain a definite idea of the regions in which nervous impulses that cause convulsions may arise, one will be in better position to inquire into the method of action of toxic substances—if such are responsible for convulsive seizures—or to search for anatomic changes if—as seems to us most probable—vascular and other anatomic changes are the important factors.

The more closely the question is studied, the clearer it becomes that the problem of the convulsive movements is only a special case of the more general problem of the functional organization of the motor system as a whole. Problems that arise in the more special field of the convulsive disorders often suggest lines of experiment in fields apparently far removed from that of the convulsive states, but the experiments in the more general field become necessary in order to gain new insight into the more special problem of the convulsions. From a close study of the character of the movements made by an animal after

3. Steiner, J.: Die Functionen des Centralnervensystems und ihre Phylogenese, Braunschweig, F. Vieweg und Sohn, 1885-1900.

4. Von Monakow, C.: Die Lokalisation im Grosshirn, Munich, J. F. Bergmann, 1914.

5. Orton, S. T.: A Pathological Study of a Case of Hydrocephalus, Am. J. Insan. **65**:229, 1908.

6. Pike, F. H.: The General Phenomena of Spinal Shock, Am. J. Physiol. **24**:124, 1909.

recovery from an experimental lesion, one can often predict the type of convulsion that will follow the use of a convulsing agent.[7]

TECHNICAL PROCEDURES USED IN THE EXPERIMENTS

Space does not permit a review of the previous work done on epilepsy, and such a review is unnecessary because of the recent publication of various monographs [8] on the subject. The work of Hughlings Jackson, Hitzig, Boyce, Horsley and Gotch and of many others is well known. For the experimental production of convulsions, some investigators have employed the method of electric stimulation of the cerebral cortex and other parts of the brain. Others, following Magnan,[9] have administered absinth to animals either by intravenous injection or by stomach. Still others have used picrotoxin or other substances as convulsing agents.

Regarded chemically, the part of the absinth molecule responsible for the production of convulsions in animals is probably an isomer of camphor found in the oil of absinth, and recently camphor monobromate has also been employed as a convulsant.

We have selected absinth as the preferable convulsing agent and have used cats for the experiments. Unless very large doses of the substance were given, the convulsions produced by the intravenous injection of absinth were uniformly clonic when the cerebral cortex was intact. At or just under the lethal dose, tonic extension of the limbs occurred with failure of the respiration at the lethal dose, the heart continuing to beat for a few minutes after the cessation of respiration. It appears, therefore, at least in the experiments on animals, that the type of convulsion may depend on the dosage: the first effect is the clonic response; larger doses cause a tonic convulsion, even when the central nervous system has not been previously injured.[10] Therefore, in all experiments with convulsing agents, the question of dosage is of considerable importance, and in our work we have been careful to keep the dosage as uniform as possible.

Our "standard" solution was made by adding 1 cc. of the oil of absinth to 19 cc. of 95 per cent ethyl alcohol, and we found that from 0.035 to 0.04 cc. per pound of body weight was the minimum convulsive dose of this standard solution for cats.

For the actual experiment the animal was placed on its back on the operating table and secured in place by tapes tied about the feet and bands passed around

7. The motor facility of animals after recovery from various lesions, taken singly and collectively, is now being carefully studied by one of us (Chappell, M. N.: On the Recovery Following Lesions in the Cerebral Cortex, Science **71**:76, 1930). The results will be presented in detail later.

8. Lennox, W. J., and Cobb, Stanley: Epilepsy, in Medicine Monographs, Baltimore, Williams & Wilkins Company, 1928, vol. 14. Muskens, L. J. J.: Epilepsy, New York, William Wood & Company, 1928. Crouzon, O.: Le syndrome épilepsie, Paris, Gaston Doin, 1929. Pagniez, A.: L'épilepsie, Paris, Masson et Cie, 1929.

9. Magnan, V.: Etude expérimentale et clinique sur l'alcoolisme, alcool et absinthe; épilepsie absinthique, Paris, Renour et Maulde, 1871.

10. The significance of the strength of the stimulus—i. e., of the degree of irritation—in the production of tonic and clonic convulsions in man is worthy of further investigation.

the neck and body just back of the fore limbs. In case one wanted particularly to watch the deportment of one or other of the limbs, that part of the body was freed from the tie tapes and allowed to move freely. A solution of procaine hydrochloride was injected into Scarpa's triangle on one side and the femoral vein exposed under local anesthesia. The internal saphenous nerve was usually cut close to its emergence from the abdominal wall so that the entire area was desensitized for the duration of the experiment. By means of a tuberculin syringe with the barrel graduated in hundredths of a cubic centimeter and a fine hypodermic needle, the desired amount of absinth solution was injected into the femoral vein, followed generally by a few cubic centimeters of 0.9 per cent sodium chloride solution in order to make certain that all of the absinth was washed out of the needle into the systemic circulation.

We shall not describe in detail the technical methods followed in the excision of parts of the brain or the technic of division of the decussation of the pyramids. The method of anatomic ablation of parts of the brain was most frequently used; foreign bodies, such as laminaria tents, were sometimes introduced into the cranial cavity through a small opening in the skull. In some of the experiments, the arteries leading to the head were temporarily clamped off for varying periods[11] so as to produce a temporary failure of cerebral function by depriving the brain of all blood excepting the modicum supplied by the anterior and posterior spinal arteries. When it was desired to keep the animal alive for long periods, the operations were done aseptically.

As the movements of the skeletal muscles constitute only a part of the total picture presented by a convulsion, we have studied the phenomena which are due probably to excitation of some part of the autonomic nervous system, such as salivation, dilatation of the pupils during the convulsion, the initial blanching and subsequent congestion of the mucous membranes, the presence or absence of pilomotor activity, the state of secretory activity of the cutaneous glands in the pads of the feet, etc. These observations are referred to only casually in this paper.

In a few experiments, the skull was opened under general anesthesia some hours before the injection of absinth and the soft tissue of the scalp temporarily sutured, so that later, by removing the skin sutures and incision of the dura, the condition of the cortical blood vessels might be observed before, during and after the convulsions.

During the absinth convulsion, the pupils dilate and for a time remain widely dilated and fail to respond to light; the hair of the back is erect and the tail is bushed; the pads of the feet begin to glisten from the moisture poured out by the glands of the skin. Micturition is frequent. The blood vessels of the cortex contract and the mucous membrane of the roof of the mouth becomes

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11. Stewart, G. N.; Guthrie, C. C.; Burns, R. L., and Pike, F. H.: The Resuscitation of the Central Nervous System of Mammals, J. Exper. Med. **8**:289, 1906. Elsberg, C. A., and Stookey, B.: Convulsions Experimentally Produced in Animals Compared with Convulsive States in Man, Arch. Neurol. & Psychiat. **9**:613 (May) 1923. Elsberg, C. A., and Pike, F. H.: The Influence of a General Increase or Diminution of Intracranial Pressure Upon the Susceptibility of Animals to Convulsive Seizures, Am. J. Physiol. **76**:593, 1926. Gomez, Liborio; and Pike, F. H.: The Histological Changes in Nerve Cells Due to Total Temporary Anemia of the Central Nervous System, J. Exper. Med. **9**:257, 1909.

almost white just before the onset of the convulsion. Protrusion of the penis is often seen in male cats. Even when the dose of absinth is insufficient to cause a generalized convulsion, the respiratory rate is greatly increased. There is often a sharp cry before the acceleration of the respiration occurs. The cry or cries cease during the period of the most violent convulsive movements, although the increased frequency of respiration may considerably outlast the convulsive movements of the muscles. After the convulsion is ended the animal may lie quietly for a time. Post mortem, the stomach is often found greatly dilated.

The effect of absinth, therefore, is not confined to the motor system for the skeletal muscles, but affects the nervous mechanisms of the autonomic system as well. This is of interest in that it shows a further parallelism between experimentally induced convulsions and the general picture of epilepsy as it is encountered in man. Further refinement of observation and studies of the experiments on animals will raise many questions concerning the clinical manifestations of human epilepsy which will require clinical investigations along new lines. Thus, certain facts we have observed in our experiments have led us to search for more data concerning the relation of the frequency of convulsions in epileptic patients during specific infectious diseases, such as pneumonia and typhoid fever, and in the protozoan infections, such as malaria. It is evident that the more closely we can duplicate the conditions seen clinically by experimental means, the more exactly will we be able to study and analyze experimentally the general state known as epilepsy.[12]

The results of the intravenous injection of absinth into normal animals are: (1) clonic and tonic manifestations in the skeletal muscles, (2) respiratory effects and (3) a group of responses due to the excitation of part or parts of the autonomic system. The question that we shall attempt to answer is: Whence come the impulses which lead to motor phenomena—whether those due to the cerebrospinal-pyramidal and extrapyramidal or to the autonomic nervous system? Are the cells of origin of the nervous impulses that originate clonic or tonic motor responses located in the cortex, or are they subcortical?

EXCISION OF CORTICAL MOTOR AREAS; EXTENSIVE BRAIN LESIONS AFTER TEMPORARY OCCLUSION OF THE CEREBRAL ARTERIES

When the cortical motor areas of both sides have been completely removed, an intravenous injection of absinth, within ten days after the operation, is followed by tonic extension of the limbs with no indication of a clonic element or, at most, by only slight indications of those motor manifestations which occur in animals when the cortex is intact [1] and are so characteristic of human epilepsy.

We have removed one entire cerebral hemisphere with the exception of a small amount of the thalamus lying immediately in front of the superior colliculus of that side, leaving the entire midbrain and the

12. The lesions produced were carefully controlled by postmortem examinations.

hemisphere of the opposite side intact. Four or five hours after such an operation, and for from three to seven days thereafter, the intravenous injection of absinth is followed by tonic convulsions on the side of the body opposite to that on which the hemisphere has been removed, while clonic convulsions appear, as usual, on the same side, i. e., on the side of the body which is controlled by the uninjured hemisphere. It seems a reasonable inference that the part of the extrapyramidal system which lies in the midbrain, or perhaps at a still lower level, is sufficient for the genesis of tonic but not of clonic convulsions.

If, instead of actual removal of part of the brain, the cerebral circulation is cut off completely [13] for a rather long period (from sixteen to fifty minutes), so that the effects of the cerebral anemia are severe, an effect which corresponds exactly to that of actual bilateral ablation of the cortical motor areas is sometimes observed. In these animals, there is the same deficiency in gait, with the fore and hind limbs sprawled out to the side and the mesial surfaces of the hind limbs and feet applied to the floor, that one sees after excision of the cortical motor areas on both sides of the brain. During the first few days after the infliction of such a severe brain lesion by either of the two methods, intravenous injections of absinth cause only tonic convulsive seizures.[14]

It has been known for many years that after the removal of the motor cortex animals will gradually and almost completely recover motor power in the affected limbs. In the human being, Hughlings Jackson was impressed with the degree of recovery that could occur weeks or months after an extensive injury to the pyramidal system.

Therefore, it was important to study the deportment of animals and the effects of absinth in the more remote postoperative period. For these experiments we used animals in which the cortical motor areas had been excised on one or both sides for from six or eight weeks to two years before.[1] After such an interval, clonic convulsions again follow the injection of absinth. It is therefore clear that during the period of recovery some change has occurred in the central nervous system—evidenced by the return of voluntary motor power, which approximates the normal, and by a change in the reaction to absinth which again is

13. Stewart, Guthrie, Burns and Pike (footnote 11, first reference).

14. Such experiments throw an interesting sidelight on the question of the duration of convulsive seizures. After a prolonged cerebral anemia, the cells of the cortex and other parts of the brain show a marked chromatolysis (Gomez and Pike: J. Exper. Med. **9**:257, 1909), and become inexcitable by absinth. Less prolonged periods of anemia (with less histologic change in the cells of the cortex) cause a greatly increased susceptibility of these cells to absinth. Clonic convulsions appear after the administration of a small dose of the convulsing agent, and this increased susceptibility may persist for days or even weeks.

like that which occurs in normal animals. It is difficult to avoid the conclusion that the same mechanism which has been responsible for the recovery of motor power is responsible also for the reappearance of clonic convulsions after the injection of absinth. These results show also that the problem of localization of the convulsive movements is a special case under the more general problem of localization of movement as a whole, and any information obtained with respect to one question will have a bearing on the other.

The results of experiments of the kind just described have led to considerable speculation as to their significance. Some investigators were led to conclude that after injury to the cortical cells of origin of the pyramidal pathways, the production of tonic convulsions in the immediate postoperative period is due to the inhibitory effect of shock on lower motor neurons, and that the possibility of producing clonic convulsions later on is due to the subsidence of shock. On the basis of such an assumption—for it must be clearly borne in mind that this is an assumption and nothing more—clonic convulsions arise from cells which lie below the cortex even though the cortex is not involved. Such a belief fails to account satisfactorily for the fact that both clonic motor perturbations and movements can be produced by electric and mechanical irritation or stimulation of the motor cortex.

The suggestion of Hughlings Jackson that after injury to one part of the central nervous system the quantity of nervous energy which flows through the remaining systems is increased so that the total is about the same as flowed through the whole system before the injury, comes very near to the truth. Jackson was familiar with the degree of recovery that could occur after a lesion in the central nervous system compatible with life, and he was a firm believer in the principle or law of the localization of function. In accordance with the views of this philosopher in neurology, our experiments have led us to conclude that immediately and soon after an injury to the cortical structures, clonic convulsions do not occur because the cells which normally give rise to them are gone. After an interval for recovery and readjustment, convulsions of a clonic type can again be produced by a convulsing agent, because of some change in other cell groups or in conduction pathways after injury to the cortical system.

HEMISECTION OF THE SPINAL CORD

The effects of experimental hemisection of the spinal cord have a direct bearing on the problem of compensation for injury, as regards both the recovery of motor power and the type of convulsive movements that occur in the limb on the side of the hemisection on administration of absinth.

It has long been known [15] that after hemisection of the spinal cord in animals, the movements of the hind limb on the side of the lesion are lost for a time, but that after from ten to fourteen days motor power is recovered, unless the injury extends across the median line into the opposite side of the spinal cord. Within this postoperative period (from ten to fourteen days) we have found that the administration of absinth will be followed by clonic responses of three limbs and by a tonic response only in the hind limb below and on the side of the hemisection. When the spinal cord has been entirely cut across, the intravenous injection of absinth never produced any kind of convulsive or other movement in the hind limbs.

The injection of absinth, after motor power has returned in the hind limb on the side of the lesion, has not, thus far, been followed by typically clonic movements of the hind limb on that side. The longest period that has, up to the present, been allowed to elapse has been one month. The results that will follow when the animals are kept for a longer period before the absinth is given cannot be stated. In the animal that lived the longest after a hemisection, there was, on administration of absinth, a flexion movement of the limb on the side of the lesion instead of the tonic extension seen after the injection of absinth during the first two weeks following the operation on the spinal cord.[16]

It would be far-fetched to assume that the pathways along which the nervous impulses travel, which cause the tonic movements of the hind limb on the side of the hemisection, are the same as those which are concerned with the production of clonic movements when the spinal cord is intact. That the mechanism concerned in the control of the motor power that has been regained is the same as that which controlled the movements of the hind limb when the spinal cord was intact is also an impossible assumption.

It seems difficult to escape from the conclusion that some other mechanism or system which bore a part of the functional burden of control of the movements of the limb when the cord was uninjured has taken over the control of such movements as are possible some months after the hemisection, and that a change has occurred in that cell system or conduction pathway whereby more nervous energy is

15. Sherrington, C. S., cited by Schäfer, E. A.: Text Book of Physiology, London, The Macmillan Company, 1900, vol. 2, p. 860. Luciani, L.: Human Physiology, London, The Macmillan Company, 1900, vol. 3, pp. 343, 331 and 574. Pike, F. H.: Some Observations on the Effects of Experimental Hemisection of the Spinal Cord, Am. J. Physiol. **85**:400, 1928.

16. Sweating of the pads of the foot on the side of the hemisection did not occur.

passing over it than did before. The location of such a pathway is still unknown, but its analysis by experimental studies may be attempted.

As already mentioned, excision of the cortical motor areas does away with the pyramidal system, leaving the extrapyramidal system anatomically, if not functionally, intact. But hemisection of the spinal cord interrupts all known efferent fibers of both pyramidal and extrapyramidal systems on that side of the cord. The only known pathways along which impulses might travel are the fibers of the direct and homolateral (if such exist in the cat) pyramidal tracts of the opposite side and possibly colliculospinal or reticulospinal paths, as well as the rubrospinal, from which the impulses might pass to the hind limb on the side of the lesion. It is extremely doubtful whether, in the cat, fibers of the direct or homolateral pyramidal tracts contribute anything to the nerve supply of the muscles of the hind limb.

Probably the operation of hemisection interrupts all the motor fibers along which impulses usually travel to the ventral horn cells of the lumbosacral cord on that side, and it would be far-fetched to assume, as Goltz has done for the reflexes after total transverse section of the cord, that the movements of the limb on the side of the hemisection are only temporarily suppressed or inhibited by the lesion, and that therefore the movements of the hind limb are controlled by some mechanism in the lumbosacral cord. If such an assumption seems unjustified for the cat, it is surely much more improbable for man. The facts derived from a study of the effects of hemisection of the spinal cord and the conclusions that must be drawn from such experiments constitute a weighty argument against the belief that the final deficiencies of function alone are to be used as an index of the functions of the injured part of the cord. They give support to the view of Hughlings Jackson that when one system is injured there is a change in the quantity of nervous energy which flows through other functionally affiliated levels or systems.

We believe that, when the spinal cord is anatomically and functionally intact, the normal motor mechanism includes the pyramidal and extrapyramidal fibers which descend from higher levels of the central nervous system. When these fibers are interrupted on one side, the system which gradually takes over the control of the motor power of the limb below the level of the lesion includes efferent pathways which must descend on the opposite side of the cord, and commissural neurons in the spinal cord below the level of the lesion. Neither shock nor inhibition are consistent with the facts, and there is nothing to support the belief in a vicarious assumption of function, i. e., that some nervous mechanism or fiber tract can take on a function with which it previously played no part or had no connection.

DIVISION OF THE DECUSSATION OF THE PYRAMIDAL TRACTS IN THE MEDULLA OBLONGATA

In the previous sections of this report, we have described the effects of injections of absinth a few days or many months after complete extirpation of the motor cortex with anatomic preservation of the extrapyramidal system and also after a partial lesion of both of these systems.

We shall, in what follows, describe the results of experiments in which the pyramidal system was partially eliminated while the extrapyramidal system was entirely preserved. This can be accomplished, if, in the lower part of the medulla, the decussation of the pyramids is severed by a median longitudinal incision, so that all possible connections between the fibers of the pyramidal tracts and the cells of origin of extrapyramidal fibers in the striatum, thalamus and midbrain, as well as the direct and homolateral pyramidal fibers, remain uninjured. By this means the crossed pyramidal fibers are completely divided, and their degeneration may be traced down to the lumbar cord in sections stained by the Marchi or Weigert methods.

The approach to the decussation of the pyramids is through the foramen magnum. The skin and muscles of the back of the neck are incised in the median line from the protuberance of the occipital bone to the spine of the second cervical vertebra. The muscles are freed from their attachment to the superior occipital ridge and occipital bone for a little distance on each side of the median line and are held apart by blunt retractors. The occipito-atlantoid ligament is freed from shreds of muscle and then incised along the border of the foramen magnum. The dura, thus exposed, is incised in the median line so that the dorsal artery of the spinal cord can be seen. A longitudinal incision is made in the median line of the spinal cord from the calamus scriptorius to about the level of the first cervical nerve roots. A thin-bladed knife is used, and the blade is pushed down until it strikes the ventral wall of the vertebral canal.

The immediate effect of the division of the decussation of the pyramidal tracts is a severe motor disability, which, however, differs somewhat from that which follows bilateral extirpation of the cortical motor areas. After the latter operation, the muscles, especially those of the hind limbs, are extremely flaccid, while after median section of the pyramidal decussation the fore limbs are occasionally spastic. Whether this spasticity is due to an incomplete division of the crossing fibers or to injury of other fiber tracts—perhaps those of the lemniscus—cannot as yet be stated.

Within from ten to fourteen days after the operation, the animal again walks around fairly well, and finally, after months have passed, the disturbance of gait that can still be observed is very slight and distinctly less than that which persists after the excision of the cortical motor areas of both sides of the cerebrum.

When the motor area of one side is excised and, after an interval of a number of weeks, the decussation of the pyramidal tracts is divided

longitudinally in the midline, the limbs on the side opposite the cortical lesion seem to be unaffected by the second operation. Within from two to three weeks after the second procedure, the animals have distinctly less motor power and control of the limbs on the side opposite to that of the cerebral lesion than of the limbs on the same side.

As was to be expected, when the most cephalic portion of the pyramidal fiber system was preserved in addition to all of the extrapyramidal fibers, the recovery of motor power was greater than when all of the fibers of the pyramidal tracts had been eliminated by cortical ablation. When, a few months after the operation, absinth was injected into these animals, clonic convulsions occurred in the fore limbs, but the movements of the hind limbs were either tonic in extension, or there was a strong tonic element in the clonic movements. When absinth was injected from six months to one year after the division of the pyramidal crossing in the medulla, the convulsions in all the limbs were again clonic and were not different from those seen in normal animals or in animals in which both cortical motor areas had been excised many months before the administration of absinth.

When the order of operations was reversed and the ablation of the motor areas was done after an interval of recovery from longitudinal splitting of the decussation of the pyramidal tracts, the immediate effects of the second operation were about as severe as those which followed lesions of the motor area with the pyramidal decussation intact. We have not yet done a sufficient number of these experiments nor kept the animals alive long enough to justify any definite statements concerning the deportment of the animals under the influence of absinth.

As in the experiments already cited in the section on hemisection of the cord, the recovery of motor power and the clonic convulsions caused by injections of absinth after motor power had returned support the contention that gradually, after the interruption of an efferent pathway, an alteration occurs in the functional capacity of some other efferent conduction tracts, "a change in the quantity of nervous energy which flows through the remaining systems after injury to one of them," as Hughlings Jackson phrased it.

MEDIAN INCISIONS IN THE MIDBRAIN

Much of our previous work has had to do with the elimination of part or all of the pyramidal system, leaving the known extrapyramidal pathways uninjured. In the experiments in which hemisection of the spinal cord was performed, however, both pyramidal and extrapyramidal fiber tracts were divided on one side of the cord. The occurrence of tonic convulsions in animals into the circulation of which absinth had been injected immediately after the ablation of the cortical

motor areas or complete removal of a cerebral hemisphere makes it probable that the tonic element of artificially produced convulsive seizures was closely bound up with the extrapyramidal motor system. It seemed important, therefore, to attempt to cause a profound lesion of the extrapyramidal, without any direct anatomic injury to the pyramidal, system.

With this object in view, we made in the midbrain of a number of animals a median longitudinal incision which extended from the superior backward to the inferior colliculus. By this midline incision, the decussation of the rubrospinal tract is severed, whereas the cerebral peduncles are not directly injured.

The technic of this procedure is relatively simple. The skull is trephined at the vertex on either side of the median line and the opening enlarged with rongeurs. The bone over the median longitudinal sinus is carefully removed so that the median longitudinal fissure between the cerebral hemispheres can be seen clearly. The dura is incised close to the median line over one hemisphere—usually the left—and raised so that the falx cerebri is clearly visible. A thin L-shaped knife, with the blade bent at right angles and projecting about 8 or 9 mm. from the line of the handle, is passed down along the falx and backward until the projecting point touches the rostral surface of the tentorium. The cutting edges of the blade are the lower and the edge rests against the tentorium. The knife is passed down along the tentorium until the tip of the blade enters the foramen lying just above the midbrain. The point of the knife is pushed backward until the upright part of the L touches the tentorium and is then pushed directly downward, sometimes until the bone at the base of the skull is felt. There is usually a slight twitch of one or both ears, and of the vibrissae as the knife is pushed down. Care should be taken to get the handle of the knife as nearly as possible in the dorsoventral plane of the animal's body and to keep the bent part of the blade in the anteroposterior axis. One, and only one, thrust of the knife is made, after which it is carefully withdrawn. The splenium of the corpus callosum is cut through on the way to the midbrain, but control experiments have failed to show any difference in the deportment under absinth, as compared with the normal, of animals in which the whole corpus callosum has been severed. There is often some hernia of one cerebral hemisphere through the incision in the dura, but control experiments have failed to show any motor effect of extensive laceration of the parietal lobe.

The immediate results of the operation are a severe effect on locomotion, some pupillary disturbances (often unsymmetrical, since the incision may involve the nucleus of the third nerve in one instance a little more than in another) and frequently, also, an inclination or torsion of the head to one side. The nose is turned to the side of the larger pupil.

The deportment of such animals under the influence of absinth is what we wish to emphasize.

In the immediate postoperative period—from three hours to a few days after the operation—typical clonic convulsions are easily elicitable.

Tonic convulsions are of late appearance or even wholly absent in some cases. One experiment is of sufficient interest to justify the citation of the protocol in full:

REPORT OF PROTOCOL

Experiment 556. Cat, weight 6 pounds (2.7 Kg.).

Date and Time		Result
Nov. 15, 1929	Median longitudinal incision of midbrain	
Nov. 19, 1929		Always lies on left side—unable to walk more than a few steps at a time. When laid on right side turns to left. There is a fine tremor in both hind legs. Some extensor rigidity with cog-wheel resistance. Pupils not especially wide with axes converging toward the top when sitting up. Bulging of head; pus escaping under pressure from puncture. Lying on back; attempt to converge brings in right eye only. Pupils small and do not react well to light. Nystagmus slow to left, quick to right and down to right malar bone. Axes are diverted at top to left.
3.00 p. m.	Absinth 0.02 c.c. per pound	Nystagmus increased by absinth. Pupils dilating. Mouth white. Few slight twitches. Tail slightly bushed.
3.13 p. m.	Absinth 0.025 cc. per pound	Nystagmus increased. Whiskers twitching. Generalized slight twitches. Flexion of right forepaw. Increased respiration.
3.23 p. m.	Absinth 0.03 cc. per pound	Pupils dilating. Salivating. Nystagmus increased. Twitches of whiskers, right forepaw and left forepaw. Bushing of tail. Pads of feet dry.
3.33 p. m.	Absinth 0.035 cc. per pound	Increased nystagmus. Twitches generalized.
3.43 p. m.	Absinth 0.04 cc. per pound	Increased nystagmus. More marked twitches. First real absinth cry.
3.53 p. m.	Absinth 0.045 cc. per pound	Big twitch. Another big twitch. Cry. More big twitches.
4.03 p. m.	Absinth 0.05 cc. per pound	Severe twitches. Real clonic convulsion. Tail very bushed. Right pupil large; left pupil small, regardless of light. Slight moisture on right foot, not on left.

Experiment 556. Cat, weight 6 pounds (2.7 Kg.).

Date and Time		Result
4.13 p. m.	Absinth 0.06 cc. per pound	Well marked twitches. No general convulsion.
4.23 p. m.	Absinth 0.07 cc. per pound	Marked twitches.
4.32 p. m.	Absinth 0.1 cc. per pound	Increased respiration. Clonic twitches. Clonic convulsion. Head drawn to left. Mouth white. Another clonic convulsion.
4.40 p. m.	Absinth 1.05 cc. total dose 0.175 cc. per pound	Tonic of ribs and glottis. Respiratory gasps. Mouth white. No typical tonic convulsion. Spasm of thorax and some of larynx. Died.

Autopsy: No meningitis. Stomach not dilated.

It may be remarked in passing that a wound infection with the presence of pus under pressure, which had been encountered in two previous cases, increased the susceptibility of animals to absinth. In one case, the minimal convulsive dose was determined before reopening the operative wound and was found to be low. After the wound was opened and the pressure relieved, the minimal convulsive dose was significantly greater. The purulent fluid itself was not responsible for the great resistance of this animal to absinth.

Other observations of interest have been made from time to time. In one animal, a tremor of the left hind leg was easily elicitable by tapping the patellar tendon in the intervals between convulsions. This faded out and was superseded by the typical clonic convulsions after the injection of absinth. The appearance of the tremor and its subsidence under absinth were exactly similar to the appearance of such a tremor and its disappearance on electric excitation of the cerebral motor cortex noted in some earlier experiments by one of us.[17] This would lead one to suspect that absinth acts in the same way as electric excitation of the cerebral motor cortex.

Ocular nystagmus, greatly increasing under the administration of absinth, was sometimes observed.

The glistening of the pads of the feet, so common in most animals after the injection of absinth, has been uniformly absent in these animals. Dilatation of the stomach has been rare or only moderate in degree. Some part of the sympathetic outflow seems to have been interrupted by the lesion of the midbrain. Respiratory effects in general have been less marked than usual.

Neither the disturbance of locomotion nor the absence of tonic convulsions can be accounted for by the extension of the lesion back to the decussation of the brachium conjunctivum. Control experiments on animals in which this decussation was severed by a knife passed up through the foramen magnum and the fourth ventricle and thrust into the caudal portion of the midbrain just below the opening of the

17. Tilney, Frederick; and Pike, F. H.: Muscular Coordination Experimentally Studied in Its Relation to the Cerebellum, Arch. Neurol. & Psychiat. **13**:289 (March) 1925; Étude expérimentale de la coordination musculaire dans son rapport avec le cervelet, Encéphale **21**:305, 1926.

sylvian aqueduct [18] have shown that the minimal convulsive and the lethal doses of absinth are low. Respiratory and autonomic effects were not decreased.

We have other animals, not yet subjected to absinth, that have survived for some months after median longitudinal splitting of the midbrain. There is more disturbance in gait and attitude of the head than one sees after an equal interval of recovery from bilateral ablation of the cortical motor areas. Spasticity of all limbs has persisted for three months and more, even though the pyramidal tract, together with its supposed inhibitory action, is intact. The logical inference is that the animal uses its pyramidal system and that the recovery is due largely to a change in the functional burden imposed on this system.

COMBINED LESIONS OF THE MIDBRAIN AND OF THE PYRAMIDAL TRACTS

The results of combined lesions of the pyramidal and extrapyramidal systems, as might be expected, are more severe than the results of lesions of either system alone. So far we have only the immediate results of both lesions made at the same time. There are two possible cases: (1) median incision of the midbrain with splitting of the pyramidal decussation and (2) median incision of the midbrain with unilateral or bilateral ablation of the cortical motor areas.

1. After a median incision of the midbrain with splitting of the pyramidal decussation, the animal lies on its side in the immediate postoperative period. It is unable to rise on its feet, but rhythmic alternating movements of the limbs soon appear. The right fore and left hind limbs move together very much as in ordinary progression. The limbs, and particularly the fore limbs, are somewhat spastic.

Three hours later, when the anesthesia has passed off sufficiently to allow a response to absinth, typical clonic convulsions are seen in the fore limbs with walking movements in the hind limbs. No tonic convulsions were observed, even with a lethal dose of absinth.

2. If both cortical motor areas had been removed at the same time that the median longitudinal incision of the midbrain was made, the animal lay on either side with only slight movements of the limbs, particularly the hind limbs, and tail. No convulsive movements of the limbs, either clonic or tonic, are observable after the injection of absinth. Swallowing movements are present, and there may be movements of the lower jaw synchronous with the respiratory movements.

Rippling of the muscles and pilomotor activity occur in the early asphyxial period following failure of the respiration from a lethal dose of absinth, and there may be well marked kicking movements at this time, although none are directly elicited by the absinth.

18. Pike, F. H., and Klenke, D. A.: Unpublished results.

Any independent action of the striatal system must, under these conditions, be slight.

OTHER EXPERIMENTAL LESIONS

Some other facts demonstrated by experiments on animals, because they have a bearing on the subject of the localization of clonic and tonic phases of convulsive seizures, should be referred to.

Transsections of the Spinal Cord and Systemic Blood Pressure.—Transverse division of the spinal cord in the upper thoracic region is followed regularly by a fall in arterial blood pressure, the amount of the fall being dependent on the level at which the spinal cord has been divided.[19] The nearer to the level of the first thoracic root (in which run the first sympathetic fibers concerned in the maintenance of blood pressure) the cord is divided, the greater the drop in blood pressure. For a short time after the cord has been cut at the level of the second or third thoracic root, the blood pressure remains low, and only a slight rise follows the occlusion of the cerebral arteries. From five to ten days later, the blood pressure is higher, on the average, than in the immediate postoperative period. Yates[20] found that occulsion of the cerebral arteries, some days after the division of the spinal cord, caused a distinctly greater rise in blood pressure than on the first day.

These experiments indicate that a conduction pathway is capable of transmitting a greater quantity of nervous energy after an interval than it can transmit immediately after a lesion to another pathway with which it was functionally associated.

Further support for this opinion may be drawn from a study of some facts obtained by experiments on the neuromuscular mechanism concerned in respiratory movements.

Division of the Vagi and Dorsal Spinal Roots.—It has been known for many years that division of both vagus nerves in the neck is followed by a profound change in the rate of respiration, which falls to one half or less of the normal, and that after a certain period the respiratory rate will often return almost to normal.[21] It has also been shown that section of the dorsal roots of the intercostal nerves will cause practically no permanent alteration in respiratory rhythm as long as the vagus nerves are intact, the only change being temporary and

19. Winkin, C. S.: An Analysis of the Nervous Control of the Cardio-Vascular Changes During Occlusion of the Head Arteries in Cats, Am. J. Physiol. **60**:1, 1922.

20. Yates, A. B.: The Mechanism of the Recovery or Maintenance of Systemic Blood Pressure After Complete Transsection of the Spinal Cord, Am. J. Physiol. **57**:68, 1921.

21. Stewart, G. N.: Some Observations on the Behavior of the Automatic Respiratory and Cardiac Mechanisms After Complete and Partial Isolation from Extrinsic Nerve Impulses, Am. J. Physiol. **20**:407, 1907.

consisting of a fall in the respiratory rate and a cessation of the costal movements.[22]

When both dorsal roots and vagi are divided within a few minutes of each other, the respiratory rate falls to only a few breaths a minute, the movements become jerky and death occurs within a short period. When the section of the dorsal roots of the thoracic nerves is done after the division of the vagi and after the respiratory rate has returned almost to normal, the effect on the respiration is just as severe as when both vagi and dorsal roots are cut at the same time.[23] It is evident, therefore, that afferent impulses from the muscles and from the lungs form part of the neural mechanism of respiration. It is reasonable to believe that compensation for the loss of the nervous impulses which travel through the vagi occurs by means of the dorsal roots in order to explain the recovery in the rate of respiration which follows after division of both vagus nerves. And the experiments just cited afford additional proof that there is no other adequate mechanism for respiration than the vagi and the dorsal roots. When both of the afferent tracts concerned in the regulation and control of respiratory movements are gone, the total effect is greater than when the function of only one has been lost. Compensation for injury to one mechanism does not come about *indiscriminately* through a vicarious assumption of function, but only through definite tracts associated or affiliated in a common function.

Still another experimental proof of the correctness of this statement is given in what follows.

Lesions of the Colliculi and the Cerebellum, and Excision of One or Both Internal Ears.—The motor disturbances which follow an injury to the inferior colliculus of one side in the immediate postoperative period are very marked.[24] After a time (about two months), however, the animal is again able to move about, but (in the ensuing five or six months—the periods during which these animals have survived) it never recovers from a marked ataxia and uncertainty or insecurity of movement. The animal, however, can walk around on the floor and is able, with some difficulty, to climb a low flight of steps.

If, now, some months after the injury to the inferior colliculus, the vestibular portion of one ear is removed, the motor disturbance again becomes much more marked and thereafter there is no improvement.

22. In advanced tabes, which has progressed until even the upper limbs are affected, no marked changes of respiratory rate have been recorded. Careful clinical observation and more data on this point are needed.

23. Pike, F. H., and Coombs, H. C.: The Organization of the Nervous Mechanism of Respiration, Science **56**:691, 1922.

24. Pike, F. H., and Klenke, D. A.: Some Effects of Experimental Lesions of the Midbrain in Cats, Am. J. Physiol. **72**:198, 1925.

The significance of such an experiment becomes clear if one appreciates that in a normal cat the motor disturbances which result from the removal of a vestibule are entirely recovered from within a few days.

In an animal kept alive for about one year after an injury to the superior vermis until it had recovered to such an extent that practically no cerebellar disturbances could be observed, the removal of one internal ear caused only transient motor symptoms. Three months later, the second vestibule was removed, and this was at once followed by a return of the tremor of the head and the general unsteadiness of gait that occurred after the injury to the vermis. Furthermore, the disturbances persisted. This was entirely different from other animals in which the disturbance caused by the removal of both vestibules was followed by recovery with disappearance of practically all of the symptoms.[18]

We are inclined to regard these results, after an injury to the cerebellum, as indicative of an increased participation of the vestibular portion of the internal ears in the maintenance and control of the position or attitude of the head. Neither inhibition nor shock is sufficient to explain the marked severity of the effect from two successive lesions, either one of which is apt to be followed by a nearly complete recession of all disturbances.

Our interpretation of the results of the experiments cited in this section may be summarized as follows: A considerable degree of recovery may occur after injury to any one mechanism or pathway through an increase of functional activity of some other mechanism or pathway normally associated or affiliated with it for the control of any particular phase of motor activity. The vagi and the dorsal roots of the intercostal nerves are normally associated in the control of the respiratory movements. The sympathetic fibers which arise from the lower thoracic segments are normally associated with those from the upper two of three thoracic segments in the maintenance and control of blood pressure. The vestibular portion of the internal ear acts normally with the collicular or cerebellar mechanisms in the control of the attitude of the head and of gait and posture.

Both cortical and subcortical parts of the brain act together for the control of motor activity and for the production of the tonic and the clonic movements of convulsions.

In the event of injury to one of a pair of associated mechanisms, the remaining one may take over a part of the work formerly done by the other, just as one horse of a team may pull a larger part of the load when the other becomes wearied or incapacitated. The method of producing combined lesions of the nervous system dates back to the work of Mayo, Magendie, Claude Bernard, Spallitta and others [25] on

25. Luciani (footnote 15, second reference, p. 331).

the differences in ocular symptoms observed when the gasserian ganglion alone was removed as compared with the symptoms observed after combined lesions of the gasserian and superior cervical ganglion of the sympathetic, but the significance of such experimental procedures becomes clear only when one recalls Jackson's view concerning the change of the quantity of nervous energy flowing through the remaining pathways after injury to one of them.

SUMMARY AND CONCLUSIONS

The results of experimentally produced convulsions in animals, with and without lesions of the pyramidal or extrapyramidal systems, must be examined in the light of the results of investigations in other fields. The belief that the recovery from the effects of a lesion of the pyramidal or extrapyramidal system is due to the change in the functional capacity of the remaining motor mechanisms is supported by observations on similar alterations of function in other systems. Just as it would be manifestly erroneous to conclude that the normal function of the afferent pulmonary fibers of the vagi in the control of respiratory movements is that which is indicated by the minimal deficiencies of function after a long period of recovery, so it would be an error to conclude that the true motor function of the pyramidal system is shown by the residual amount of motor disability. In the one instance one would be reckoning without the dorsal roots of the thoracic nerves, and in the other without the phylogenetically older motor mechanisms and their ability almost completely to resume an old task.

The persistence of locomotion after elimination of the rubrospinal system so long as the pyramidal system is intact means either that this motor facility is associated with the function of the pyramidal tract or that neither rubrospinal nor pyramidal tracts have much to do with movement. The greatly increased severity of the motor symptoms when both systems are injured shows that, as a matter of fact, both pyramidal and rubrospinal systems are concerned with the control of movement.

It is still uncertain how much functional importance in locomotion is to be attached to uncrossed descending tracts from the striatum,[26] midbrain [27] and reticular formation. It has been shown [28] that, so far

26. Morrison, L. R.: Anatomical Studies of the Central Nervous System of Dogs Without Forebrain or Cerebellum, Haarlem, de Erven F. Bohn, 1929.

27. Rasmussen, A. T.: Experimental Demonstration of the Entire Course of Four Descending Tracts by a Single Alcoholic Injection in the Midbrain of the Cat, Proc. Soc. Exper. Biol. & Med. **20**:104, 1922-1923.

28. Coombs, H. C.: The Effect of Division of the Dorsal Roots of the Cervical Nerves upon the Rate and Magnitude of Diaphragmatic Respiratory Movements, Proc. Soc. Exper. Biol. & Med. **27**:196, 1929; The Effect of Unilateral Section of the Midbrain upon Costal Movements of Respiration, Science, to be published.

as its relation to costal movements of respiration is concerned, the control of the region of the midbrain over respiratory movements is ipsolateral.

We believe that, normally, the pyramidal is the main motor system, which is responsible for the clonic convulsions that occur when the pyramidal system is entirely or almost entirely intact. The ability to produce only tonic convulsions immediately after an injury to the pyramidal system is not to be attributed to any effect of shock or inhibition on lower motor mechanisms, but to the fact that insufficient time has elapsed for a change in the amount of function of which these mechanisms are capable. After a period during which a readjustment of function can occur, clonic convulsions may arise from lower, older mechanisms after an injury to higher, phylogenetically newer mechanisms. This is not necessarily to be interpreted as evidence that the older mechanisms play the most important rôle in the production of clonic convulsions when the newer mechanisms are intact.

The results after hemisection of the spinal cord, taken in conjunction with the evidence from experiments in other fields, leave little doubt that changes in the functional capacity of pathways and mechanisms can and do occur after an injury to a mechanism normally related in function.

The fact that clonic convulsions may occur in infancy, before the myelinization of the fibers of the pyramidal tracts is well advanced or complete, does not come in conflict with but rather supports the views that we have set forth. Thom and Southard [29] found a history of epileptic convulsions before the age of 1 year in 5.5 per cent of their cases which came to autopsy and in which the brain appeared normal and in 11 per cent of cases in which the brain tissue was found diseased or injured. It is well known that—from various causes—clonic convulsions may occur in infants during the first days after birth. Before the pyramidal fibers have become myelinated and have attained their full functional capacity, clonic convulsions arise from lower motor mechanisms. With the attainment of its full function, the pyramidal system assumes general control of the movements in ontogenetic development just as it assumes control of such motor activity in phylogenetic development.

If one accepts as correct the statement that a change in the functional capacity of a system—the alteration in the quantity of nervous energy flowing through it—may and does occur, it is possible to understand why the effects of a lesion of the pyramidal system are definitely less when the cells of origin of its fibers and the course of the fibers down to the lower (phylogenetically older) motor mechanisms are spared

29. Thom, D. A., and Southard, E. E.: An Anatomical Search for Idiopathic Epilepsy, Rev. Neurol. & Psychiat., October, 1915 (reprint, p. 5).

than when the whole of the pyramidal system is affected. When the decussation of the pyramidal fibers is split longitudinally, the cortical mechanisms can still retain their control over the lower motor systems and the motor deficiencies are definitely less than when the cortical motor areas have been removed anatomically. A greater degree of compensation is possible through the lower motor mechanisms under the first set of conditions than under the second.

Available evidence leaves no room for doubt that during vertebrate development a shift of function toward the anterior end of the central nervous axis has occurred. Profound changes in motor nerves, muscular mechanisms and central nuclei of termination can be shown definitely in the respiratory mechanism in the transition from fish to mammal.[30] Anatomically, the changes that have occurred are still obscure. Experimentally, the magnitude of the changes becomes clear. Applying the argument drawn from a consideration of the changes in the central nervous system during vertebrate development to the case of the motor mechanism in man and the convulsive disorders which arise from it, one can readily see why a lesion of the pyramidal system should have a more profound and more permanent effect in man than in cats. Motor control has been taken over more and more completely by the pyramidal system in the higher types. The definitely decreased degree of recovery possible after a lesion of the pyramidal system in man is not necessarily to be interpreted, as Goltz insisted, as evidence of a greater and more permanent effect of shock in man as compared with the lower animals, but it may be interpreted much better on the basis of the assumption or acquisition of a more complete control of the general movements by the pyramidal system in man, owing to the wandering of function from lower, older to higher, phylogenetically newer motor mechanisms. These considerations indicate with great probability that in man, when the central nervous system is otherwise intact, clonic convulsions are of cortical origin.[31] The fact that clonic convulsions may appear in man after injury to the cortical mechanisms cannot be adduced as evidence in favor of their origin in the lower mechanisms when the cortical mechanisms are intact.

When we grasp the significance of Hughlings Jackson's view that a change in the quantity of nervous energy flowing through a given pathway or system may occur after injury to some related system, we are better fitted to understand his position with reference to cerebral localization. He was convinced of the truth of his view that a change in the quantity of nervous energy flowing through a given pathway

30. Springer, M. G.: The Nervous Mechanism of Respiration of the Selachii, Arch. Neurol. & Psychiat. **19**:834 (May) 1928.

31. Schäfer, E. A.: Text Book of Physiology, London, 1900, vol. 2, p. 718. Luciani (footnote 15, second reference.)

might occur when some other functionally related pathway was injured, and he may well have recognized that, if there were no such changes in the functional capacity of the remaining pathways after injury to one or more, the whole fabric of localization must fall.

His views that the cortical motor mechanisms acted together with the lower mechanisms as one motor system are borne out by the effects of longitudinal splitting of the decussation of the pyramids. How else could the recovery be greater under these conditions than when the motor area has been removed bilaterally?

From the facts thus far obtained from our experiments, it seems improbable that the direct (and homolateral) pyramidal tracts (even if they exist in the animals) are sufficient to explain the differences. How else than by a wandering of function from lower to higher and phylogenetically newer motor mechanisms can one explain the much more severe effects of lesions of the cerebral hemispheres in man than in the lower vertebrates? This wandering of function from the lower, older to the higher, newer mechanisms in vertebrate development constitutes the biologic evidence for cerebral localization of function.

From all of the facts presented in this paper, the following conclusions seem justified:

1. Clonic convulsions arise from the cerebral motor cortex when this is anatomically and functionally intact.

2. Tonic convulsions arise from the lower motor mechanisms in the period immediately succeeding an injury to the cortical motor mechanisms. After the lapse of sufficient time, clonic responses may be elicited from them. This is, however, not evidence that clonic convulsions may and do arise from the lower motor mechanisms when the cortical mechanisms are intact.

3. Tonic convulsions are absent in the early postoperative stages in animals in which the midbrain has been split longitudinally in the median line, while clonic convulsions persist if the pyramidal system is intact.

4. All parts of the motor mechanism act together as one system when the brain is intact. It does not seem probable that when the whole motor system is intact, one part of the mechanism gives rise to movements of one type and some other part of the mechanism independently gives rise to movements of another type.

THE ANATOMIC SUBSTRATUM OF THE CONVULSIVE STATE*

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The first question which the clinician puts to the anatomist is important in the problem of epilepsy: What is the substratum of the process? Can this process be diagnosed anatomically, and can it be defined or limited anatomically? It is known that anatomy has done much to divide epilepsy into many single entities. It has helped to classify more and more cases in the group of "symptomatic" epilepsy, not only as previously by the gross anatomic processes, but also by the finer, histologically peculiar changes. The main question now is: Has a group remained after this division of epilepsy which one can designate as "genuine" epilepsy, from the anatomic point of view? To date, one is unable to do this. One can say only that one finds many cases in which histologic investigation discloses nothing or nearly nothing that is characteristic. One must admit, however, *a priori* that one possibly may be able to recognize changes with new methods and with more experience. So one must admit that a genuine form of epilepsy may exist.

Pathologic anatomy, however, cannot give support today to the view that there is a "genuine" epilepsy. To the present, it has been a futile and negative attempt on the part of anatomy to define genuine epilepsy in the sense of Lennox and Cobb. They define epilepsy in their excellent book as "a syndrome rather than a disease entity." In this book, they viewed all the facts and theories critically. Along with the brain, other organs, especially endocrine organs and the circulatory system, were much investigated. I do not need to go into detail about this, for I have nothing to add to what Lennox and Cobb have already said.

Since you have kindly invited me to speak of my own investigations I can limit myself to them. I would like to tell you how I have tried to interpret functionally certain anatomic observations in the epilepsies.

Pathologic anatomy is primarily morphology. But from this morphology it must also attempt to arrive at conclusions about functional processes which lead to anatomic changes in the tissue. For a long time, and particularly today, one strives to obtain a continuous series of

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phases of the respective process from its end back to its beginning. This pathogenic review of the development of a process back to its beginning leads finally to the earliest stage. This affords a view beyond the morphologic into the physiologic or pathophysiologic: into the how of the earliest mechanism which determines the tissue change, but not into the still more remote causal *why;* for it lies mostly beyond the ability of pathologic proof to demonstrate the etiology. Therefore I wish to stress at the beginning that one cannot expect to obtain a knowledge of the causes of epilepsy from anatomic studies, but one can draw conclusions as to certain functional phenomena which immediately precede the epileptic seizures. In the explanation of these phenomena I do not wish to deviate from the guiding principle of Lennox and Cobb, which they express in the following words: "Explanation of unseen things there must be, but such deductions must, if possible, be based on evidence."

The aforementioned method of pathogenic study, the picturization of the anatomic state from its end back to its beginning, I have followed in the study of Ammon's horn sclerosis, the old, well known, but variously explained observation. This sclerosis usually looks like a thick glial proliferation in locally circumscribed parts of Ammon's horn. In the Nissl picture, the change appears as a loss of ganglion cells in definite areas. These defects in the nerve-cell picture correspond to the increase of the glia fibers in the previous picture. This is the usual observation. One is dealing with an end state. The histologic analysis of such a sclerotic atrophy cannot give any explanation of the process which produced this atrophy. I have found now, however, the earliest states, the first changes in this process, in various cases—in cases of "genuine" epilepsy, as well as in many different examples of symptomatic epilepsy due to trauma, intoxications, eclampsia, whooping cough eclampsia and diffuse cerebral processes.

I wish to show, first, a general view of a fresh loss of nerve cells on the border between the attacked foci and the normal contiguous tissue (fig. 1). Most of the cells are gone; some are still recognizable as shadows. In the place of ganglion cells, one sees proliferated glia cells of the rod form, which Nissl described thirty years ago and which today are called Hortega cells. With greater magnification, one sees here pale, shadow-like ganglion cells, which I have called "ischemic" ganglion cells because of their pathogenesis. They are surrounded by proliferated Nissl "Stäbchenzellen." These mark the borders or the location of the disintegrating ganglion cells. In figure 2 are to be seen these ischemic ganglion cells among normal cells on the border between the normal and the diseased zones. One can see these cells better in the usual hematoxylin-eosin preparations. The ischemic ganglion cells still stain intensely with eosin when the necrotic cell body is already unstained

in the Nissl preparation. One sees its sharp three-cornered form and narrow body in comparison with the normal cell, and the marked disintegration of the nucleus.

I find an important help for this pathogenic analysis of the changes in Ammon's horn in the changes in the cerebellum, which are similar in principle. These cerebellar changes are about as frequent as the changes in Ammon's horn in the most varied epilepsies. Here also one usually finds the sclerosis: a proliferation of the fibroglia in the molecular zone. This replaces the degenerated nervous tissue substance, and above all, the loss of the Purkinje cells, the shrinkage of the molecular

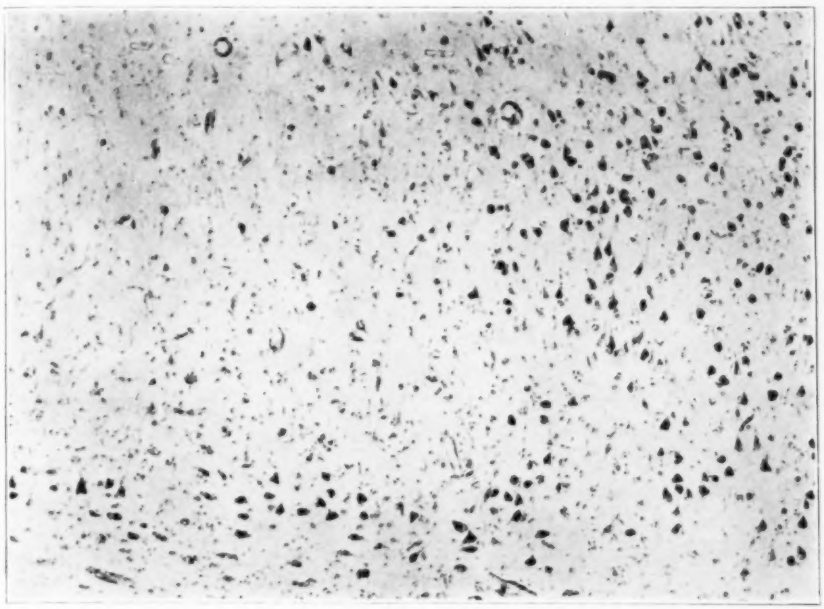

Fig. 1.—Loss of nerve cells on the border between the attacked foci in Ammon's horn and the normal contiguous tissue.

zone, and the increase in the number of Bergmann glia cells in a thick row. Here also one can find the earliest changes, often close to old cellular losses in other places. These fresh losses are especially well marked by a branchlike network of proliferating glia cells (fig. 3). With greater magnification one can see also certain details—the relations between the cells and the surroundings and replacement of Purkinje cells by glia cells. This is the same as in Ammon's horn.

These pathogenic analyses receive their peculiar value only in their relation to the clinical facts, for I found the fresh changes in Ammon's horn and the cerebellum after epileptic seizures and states. In my

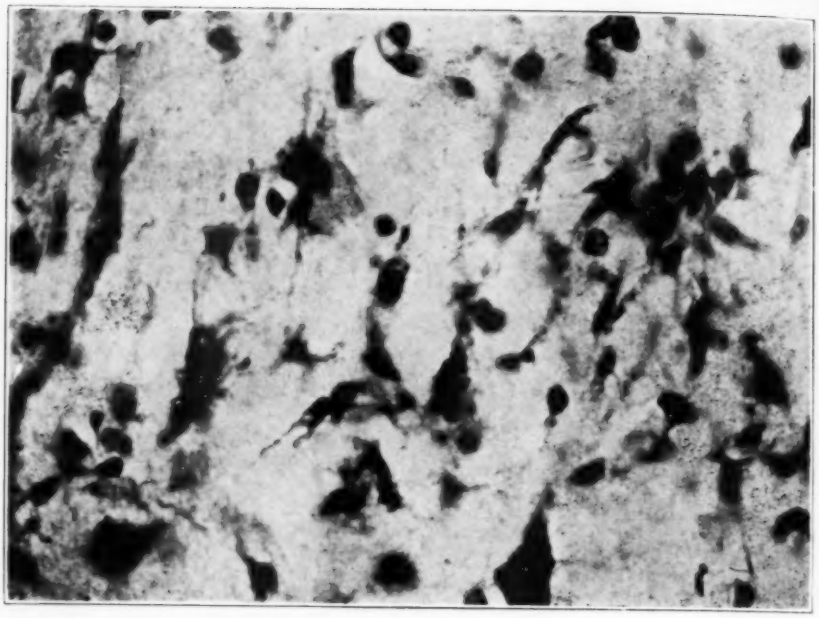

Fig. 2.—Ischemic ganglion cells among normal cells on the border between the normal and the diseased zones.

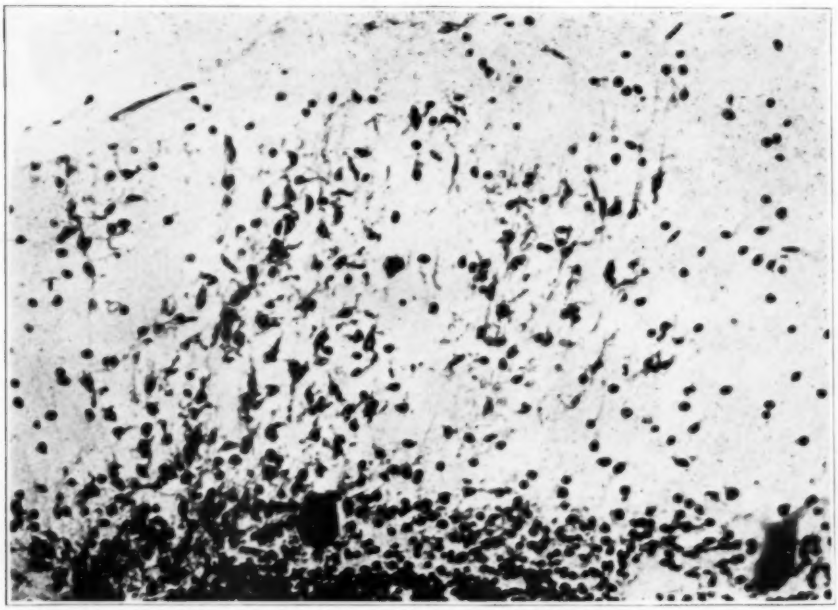

Fig. 3.—Section showing relations between the ischemic ganglion cells and their surroundings, and the replacement of Purkinje cells by glia cells.

opinion, they are somehow related to the seizures—to the mechanical factor responsible for the seizure. The more one seeks, the more often does one find recent or older changes in both these places—in so-called genuine epilepsy, as well as in the symptomatic forms, in traumatic epilepsy, in tumors with seizures, in Huntington's chorea with attacks and in atrophy of the hemispheres with attacks. Different as the various processes are in their fundamental causes, they nevertheless agree in this anatomic change—just as they all correspond clinically in the symptom of the attack in spite of all their other variabilities.

In the discoveries just shown, it is of the first importance that the histologic quality of the changes is not dependent on the etiologic process itself, for that process does not affect the characteristic location of the lesion in Ammon's horn. On the contrary, it is the same histologic picture that one finds in all the different symptomatic epilepsies with their different anatomic substrata.

I believe that these facts show that the similar changes demonstrated are closely related to the similar symptom of the epileptic attacks, and that circulatory disturbances play a rôle here. The type of the ischemic ganglion cell changes proves, in my opinion, their genesis. But I believe that objections can be raised to this, and therefore it is important that one should prove this genesis in other ways. I found exactly the same changes in exactly the same places in Ammon's horn in true organic obstruction to the circulation. I show this in a picture of endarteritis tuberculosa (fig. 4). One recognizes the recent loss of nerve cells which is several days old. The circumscribed defect here is the same as that shown in figure 5 from a case of symptomatic epilepsy with a final epileptic state; it presents a corresponding fresh loss of cells in the same place, in Ammon's horn.

I could complete this demonstration with pictures of arteriosclerosis, thrombosis and embolism. But the pictures already shown are sufficient. One sees, therefore, that organic occlusion of the circulation produces changes like those seen in epilepsy in similar locations. I conclude from this that in epilepsy, also, an impediment to the circulation must have been present, and since organic impediments are absent, the circulatory function must at some time have been disturbed.

The answer to the question why Ammon's horn and the cerebellum usually show a visible effect from this circulatory disturbance would take me too far afield. I believe that the local, relatively unsatisfactory blood-vascular supply to these parts is responsible for this, so that in partial hindrances to the blood supply these especially poorly supplied parts suffer first. Whereas in other parts of the brain with a better blood supply a compensatory reaction to the disturbance is possible.

The anatomic pictures allow one to conclude that vasomotor disturbances are effective in the mechanism of the epileptic attack. Thus,

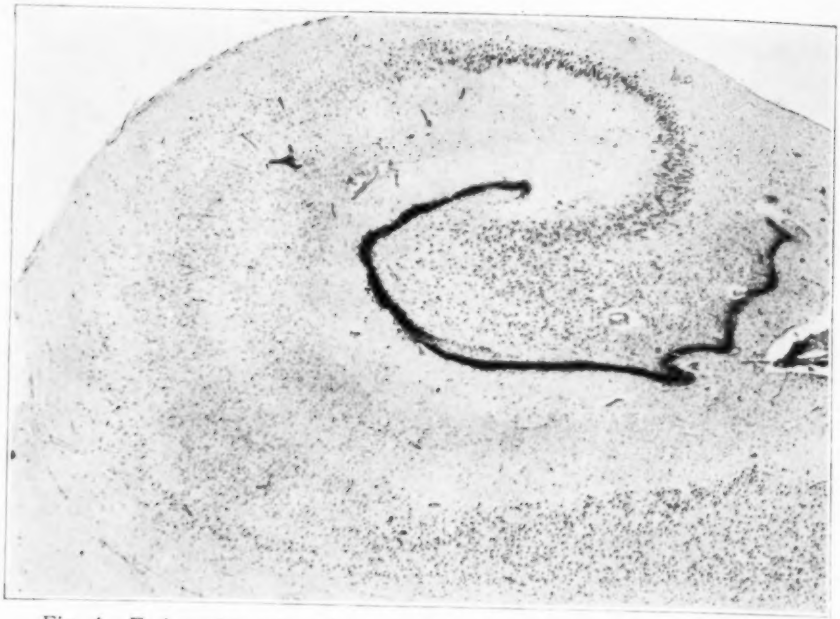

Fig. 4.—Endarteritis tuberculosa, showing loss of cells in Ammon's horn.

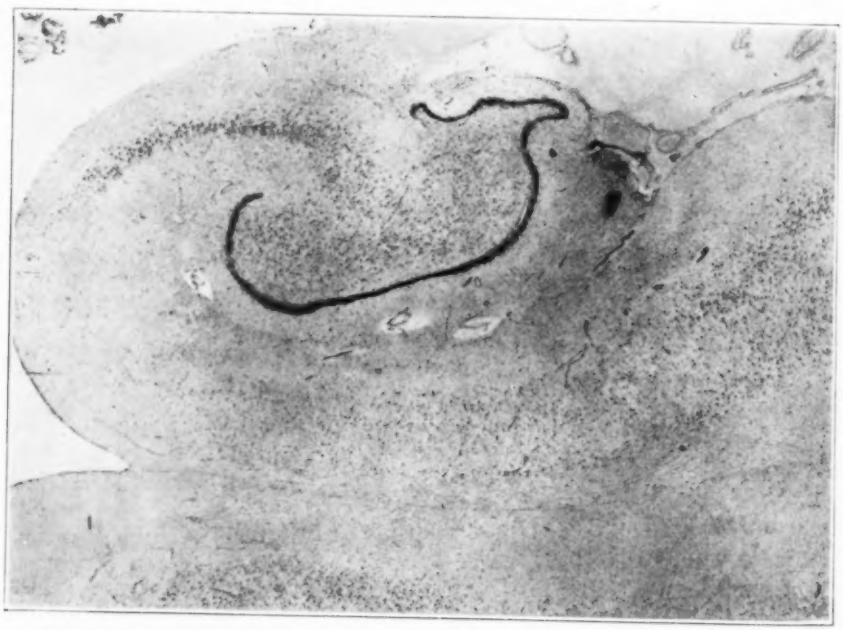

Fig. 5.—Symptomatic epilepsy, showing the same loss of cells in the same place in Ammon's horn.

the anatomist comes back to the old vasomotor theory of the attacks. Since he finds no evidence of stasis, he believes in the action of vasospasms. The anatomist thus comes with his own methods and in his own way to a completion of the observations which neurosurgeons, particularly in America, have made. I refer to the sudden anemia and decrease in the size of the brain at the beginning of the attacks, seen in the course of exploratory craniotomies. I refer to the observations of Horsley, Dandy, Hartwell, Kennedy, Horrax and Leriche. Many other clinical observations support this view; for example, the pallor of the skin and of the retina, and the association of vasomotor instability with epilepsy. I shall mention one thing more, since it can also be established anatomically: myocardial changes without organic changes of the coronary arteries. Since Gruber and Lanz described an anemic focus in the myocardium after status epilepticus, one of my co-workers, Dr. Neubürger, has regularly investigated the hearts of young, non-arteriosclerotic epileptic patients. He found after epileptic attacks a recent destruction of muscle elements.

In closing, I repeat that these observations can tell one nothing about the essential causes of epilepsy. On the other hand, these investigations allow one to draw conclusions from the morphologic about the pathophysiologic, i. e., about the mechanism of the attacks.

THE EFFECTS OF ANEMIA ON THE CEREBRAL CORTEX OF THE CAT*

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This inquiry into the effects of cerebral anemia has been undertaken for three reasons: (*1*) to produce experimentally the lesions in the cerebral cortex that many observers have described as characteristic of cerebral anemia in man; (*2*) to obtain additional evidence as to the endurance of anemia by cerebral nerve cells, and (*3*) to attempt to correlate these lesions with the symptoms that may occur as the result of anemia.

Spielmeyer,[1] in recent years, has investigated the pathologic changes in the brains of patients dying from various forms of vascular disease which are supposed to produce cerebral anemia. He has described lesions, consisting of many shrunken, homogeneous, dark-staining cells that he considers characteristic of cerebral ischemia. We have attempted to reproduce this picture in animals by shutting off the blood supply to the brain for various periods of time.

Cannon and Burket (1913)[2] briefly summarized the literature relating to the time that the cortical cells and other parts of the nervous system can endure anemia. They confined their experiments to the myenteric plexus and produced satisfactory evidence to show that few or no pathologic changes occur until after three hours of anemia. They did no work of their own on the capacity of other parts of the nervous system to withstand anemia. They referred to only three groups of experiments as their authority for the time the cerebrum can endure anemia, and they made no attempt to evaluate the methods used by these workers. Consequently, we have paid particular attention to this aspect of cerebral anemia.

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* From the Neuropathology Laboratory, Harvard Medical School.

* This work was made possible by a grant from the "Committee on Electric Shock" of the New York Edison Company.

1. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922; Vasomotorisch trophische Veränderungen bei zerebraler Arteriosklerose, Monatschr. f. Psychiat. u. Neurol. **68**:605, 1928.

2. Cannon, W. B., and Burket, I. R.: The Endurance of Anemia by Cells of the Myenteric Plexus, Am. J. Physiol. **32**:347, 1913.

It has been stated by many investigators and recently by Lennox and Cobb (1928) [3] that an anoxemia of the brain if severe and prolonged enough is regularly followed by convulsions. This suggests the importance of the old hypothesis that disturbances in the cerebral circulation, resulting in local ischemia, may be a factor in the etiology of epilepsy. To discover what histologic lesions of the cortex are consistently produced by ischemia is of importance in understanding the asphyxia of electric shock, carbon monoxide inhalation, drowning and many other common accidents.

REVIEW OF LITERATURE

Leonard Hill (1896),[4] de Buck and de Moor (1901),[5] and Pike and Stewart (1906-1909) [6] have reviewed the literature on cerebral anemia up to the time of their papers. Since 1909, most of the experimental work has been on the physiologic effect of cerebral anemia with only occasional reference to histopathology. For the sake of simplicity we have divided this summary of the literature into two parts: One deals with the physiologic effects of cerebral anemia and the other with the histopathologic changes associated with these effects.

Physiologic Aspects.—The effect of ligature of the carotid artery has been somewhat understood from the earliest days. According to Hill,[4] the first important experiment of this type was performed on a dog by Astley Cooper (1836), who tied the vertebrals at their origin from the innominate and left subclavian arteries and at the same time ligated the carotids. He noted that spasms resulted immediately and that respiration ceased. Magendie and Poiseuille (1837) [7] reported similar experiments. During the rest of this century, ligation of the four cerebral arteries was performed by many investigators, and the accompanying physiologic changes were fairly well worked out, such as the importance of medullary centers in the maintenance of life. In 1878, Mayer [8] repeated the experiments of Cooper and Magendie with unusual care and described the results in detail. Not much work was done on

3. Lennox, W. G., and Cobb, S.: Epilepsy, Medicine Monographs, Baltimore, Williams & Wilkins Company, 1928, vol. 14, p. 36.

4. Hill, Leonard: The Cerebral Circulation, London, J. & A. Churchill, 1896.

5. De Buck, D., and de Moor, L.: Lésions des cellules nerveuses sous l'influence de l'anémie aiguë, Le Névraxe **2**:2, 1901.

6. Stewart, G. N.; Guthrie, C. C.; Burns, R. L., and Pike, F. H.: Studies in Resuscitation, J. Exper. Med. **8**:289, 1906; **10**:490, 1908. Gomez, L., and Pike, F. H.: The Histological Changes in Nerve Cells Due to Total Temporary Anemia of the Central Nervous System, ibid. **11**:257, 1909.

7. Magendie, F., and Poiseuille, H.: Leçons sur les phénomènes physiques de la vie, Paris, 1837, p. 12.

8. Mayer, S.: Sitzungsb. d. k. Akad. Wissensch. (Aft. 3) **73**:85, 1874; Medicin. Centralbl. **16**:579, 1878.

the histopathologic changes produced by cerebral anemia.[9] De Buck and de Moor [5] also carefully reviewed the literature and repeated experiments on the spinal cord. They concluded that Nissl's stain was the most delicate method available for demonstrating early histologic changes resulting from anemia. The results of these experiments, especially in relation to the time that various nerve centers can endure anemia, have proved difficult to evaluate, because no one has devised a method for measuring reliably the degree of cerebral anemia. Even when the innominate and left subclavian arteries are ligated, complete anemia does not occur because of the rich anastomoses of the intercostal vessels with the spinal arteries. Hill and others have shown that these anastomoses are so extensive in many animals, especially dogs, that they cannot be killed by permanent ligation of the innominate and left subclavian arteries. Hill has stated that horses and goats can be killed by ligation of the carotid arteries alone, but has presented no experimental evidence on this point. He found that one of three cats died after ligation of the four main cerebral vessels, and that monkeys reacted in about the same manner. Hill emphasized the fact that the least trickle of blood can maintain the activity of nerve cells for a surprisingly long period. This observation has been confirmed repeatedly by numerous observers. Even stagnating blood about nerve cells prolongs their life.

Segalas d'Etchepare (1924) [10] and Batelli (1900) [11] found that after ligature of the abdominal aorta the struggles of animals lasted longer when the vena cava had been tied than when it had not. Cannon and Burket [2] reported that ligatures carefully tied about the colon and stomach do not produce serious impairment of function in these organs even after seven hours, but when blood is squeezed out of them by pressure between glass plates, activity ceases after three hours, and definite changes occur in nerve cells. Roberts (1924) [12] demonstrated that even after ligation of the four cerebral vessels some pressure is maintained in the circle of Willis. In addition, Brown (1916) [13] has shown that spinal vessels readily carry dyes to and from the brain. Even in experiments in which the contractions of the heart have been stopped, such as those of Batelli,[11] anemia has not been complete, for Pike and

9. Extensive histologic studies, however, were made on the spinal cord, after ligation or digital compression of the abdominal aorta. This work will be reviewed under histopathologic aspects.

10. D'Etchepare, Segalas: Sur quelques pointes de physiologie, J. de physiol. expér. **4**:287, 1824.

11. Batelli, F.: Le rétablissement des fonctions du coeur et du système nerveux central après l'anémie totale, J. de physiol. et de path. gén. **2**:443, 1900.

12. Roberts, F.: Experimental Study of Cerebral Anemia, J. Physiol. **59**:99, 1924.

13. Brown, E. D.: Artificial Circulation After Isolation of Mammalian Brain, J. Pharmacol. & Exper. Therap. **8**:185, 1916.

Stewart [6] have pointed out that slight fibrillations of the heart may maintain a small amount of blood flow; moreover, one cannot be sure the heart has ceased to function except by direct inspection. These observations readily explain the reported recovery of nerve cells after long periods of anemia and also account for the discrepancies in the results of various experimenters. The phenomenal clinical cases of resuscitation, hours after apparent death, can likewise be thus accounted for. Furthermore, any errors in experiments on the time cerebral cells can endure anemia probably have been on the side of making the period too long. Consequently, Pike, Stewart and others (1906-1909) have rightly discarded the records of recovery after prolonged periods of anemia. A. Chauchard and B. Chauchard (1928),[14] in recent studies on chronaxie in relation to cerebral anemia in dogs, have redemonstrated the ability of the spinal arteries alone to maintain some degree of cerebral circulation.

Mayer,[8] who appears to have done careful work, concluded that from ten to fifteen minutes of cerebral anemia is sufficient to damage the brain permanently. Batelli [11] stopped the heart by means of an induced current and, in spite of the fact that there must have been much stasis of cerebral blood and possibly a slight flow from a fibrillating heart, recorded inconstant recovery after fifteen minutes and no recovery of animals after twenty minutes. Pike, Stewart and Guthrie (1906-1909) [6] ligated the innominate and left subclavian arteries in a large series of cats. They found that a good occlusion of these vessels, prolonged over fifteen minutes, permanently abolishes functional activity of the cerebral and medullary centers. The cerebral cortex was found to be more sensitive than the medullary centers. In their series of ninety-three cats (1906), five animals recovered completely after an occlusion period of seven minutes, only one after fifteen minutes and none after twenty minutes. In this paper they paid little attention to mental symptoms. They concluded that over fifteen minutes of cerebral anemia results in death no matter what methods of resuscitation may be used. They have reported their experiments in sufficient detail to indicate the accuracy of their conclusion that this figure is the maximum limit, and that probably if anemia were really complete the endurance period would be much shorter.

The technic used in these experiments appears to have been unusually good. After cats were etherized, the authors dissected out the innominate and left subclavian arteries and passed ligatures about them, proximal to the origin of the vertebral arteries. During the period of occlusion of the vessels, artificial respiration by means of a tracheal

14. Chauchard, A., and Chauchard, B.: Rôle des collatérales des artéries vertébrales et carotides dans l'irrigation de l'écorce cérébrale, Compt. rend. Soc. de biol. **99**:1628, 1928.

cannula was employed and was continued after restoration of cerebral circulation until normal respiration had reappeared. In many experiments the heart was kept going, if necessary, for hours by this artificial means. They give excellent reports of the early and remote effects of cerebral anemia, which may be summarized as follows: Immediately after occlusion of the innominate and left subclavian arteries in a cat, the nose and mucous membranes become pale, the animal stiffens out, and respiration increases in rate and then develops irregularities, and at from thirty seconds to two minutes stops entirely. Reflexes, including the corneal reflex, disappear and the pupils dilate. The heart speeds up at first and then, as the vagus center is affected, becomes temporarily slowed. The blood pressure, as the pulse rate becomes slow, begins to rise. (They record the blood pressure curves in detail.) The picture presented at the close of a typical occlusion is an animal with widely dilated pupils, lax and sunken cornea, motionless eyelids, no tear secretion, bloodless mucosa of the nose and mouth, relaxed muscles, no voluntary respiratory movements and low blood pressure. The heart beat is slow and weak and may stop. These authors consider the immediate cessation of respiration as the most reliable indication of a complete occlusion. After the vessels are released, provided the occlusion period has not been too long (from ten to twenty minutes) the mucous membranes immediately become pink and respiration returns suddenly, usually within from two to sixty minutes if it is to return at all. Reflexes and normal intra-ocular tension return more gradually. Convulsions may occur at any time from a few minutes to several days after restoration of circulation. These convulsions are described as beginning usually with extensor rigidity, quickly changing into a less regular type of tonic convulsions and then into the clonic type.

Pike and his colleagues have described a variety of late symptoms in different animals, especially those in which the occlusion period was longer than eight minutes. Some developed a spastic gait; others became peculiar in their behavior, developing yowling spells, running fits or "dementia." Blindness occurred in one case. Many cats failed to eat and had to be tube fed. Not much emphasis is placed on extensor rigidity or on the impairment of intelligence. No reference is made to convulsions occurring during the period of occlusion of cerebral vessels.

The experiments of Stewart, Pike et al. have been repeated by many workers, but only in an effort to elucidate physiologic principles not relevant to our problem. Winkin (1922) [15] has adequately reviewed this literature.

The numerous clinical and pathologic studies that have been made on cerebral anemia and asphyxia have furnished some indication of what

15. Winkin, C. S.: Cardiovascular Changes During Cerebral Anemia, Am. J. Physiol. **60**:1, 1922.

one might expect to find in experimental cerebral anemia in animals. In connection with asphyxia neonatorum, cerebral anemia has been considered as an important factor. Ford (1928) [16] briefly reviewed the literature on this subject and concluded that trauma is more important than anoxemia. He asphyxiated a series of cats by placing them in a bell jar from which oxygen was quickly washed out by the introduction of nitrogen. From three to five minutes after the cessation of respiration, the animals could be resuscitated, but after this period artificial respiration of various forms proved ineffective. This appeared to be due to the failure of the heart, which could not be revived by epinephrine, massage or other cardiac stimulants. Animals that were revived, recovered promptly and completely. A second series of cats was exposed for a long period, usually twelve hours, to an atmosphere of from 5.5 to 6 per cent oxygen (the animals could be kept alive for only a short time when the oxygen was below 4.5 per cent). In this atmosphere the cats were drowsy but could always be roused. When returned to room atmosphere, they were unable to stand for half an hour and would yowl for some time. All animals had completely recovered at the end of twenty-four hours. Anoxemia produced by this method is probably not so severe as that produced by ligation of the four main cerebral arteries while the heart is maintained in normal condition by artificial respiration.

Martin (1918) [17] placed rabbits in the low oxygen chamber of Kolls and Loevenhart. These animals became drowsy in an atmosphere of 10 per cent oxygen; in 7 per cent oxygen they refused to eat; in 6 per cent oxygen they developed peculiar chewing motions and usually lay on one side with the head thrown back; they experienced difficulty if they made an effort to sit up. A series of rabbits was exposed to 6 per cent oxygen for 260 hours, and of these only one became paralyzed and one developed convulsions. The anatomic changes produced by these experiments will be described in the following section.

Histopathologic Changes.—The great majority of studies on the effects of anemia on nerve cells have been made on the spinal cord. These experiments have been carefully reviewed by de Buck and de Moor.[5] Gomez and Pike [6] have covered the literature from 1901 to 1909. The method of producing anemia of the cord used by most of these workers is the classic one devised by Stenson (1667) [17a] and Swammerdam (1687).[17a] The technic consists of passing a ligature about the spinal cord and aorta at the level of the fourth lumbar vertebra. The aorta is thus compressed against the spine. This method, due

16. Ford, F. R.: An Experimental Investigation into the Effects of Asphyxia on the Brain, Bull. Johns Hopkins Hosp. **42**:70, 1928.

17. Martin, H. G.; Loevenhart, A. S., and Bunting, C. H.: Morphological Changes in Tissues of Rabbit as Result of Reduced Oxidation, J. Exper. Med. **27**:399, 1918.

17a. Quoted by de Buch and de Moor (footnote 5).

to anastomosis of vessels, produces a variable and incomplete degree of anemia, but if the ligature is left on long enough, changes eventually occur in the cells of the spinal cord. De Buck and de Moor have reviewed these experiments exhaustively and compared them with their own observations. They state that Nissl's method of staining nerve cells is the most sensitive and satisfactory for detecting early changes as a result of anemia. On this basis they eliminate the work done before the time of Nissl as of uncertain histologic value. Their paper may be summarized as follows: An animal has to survive at least three hours after the beginning of the occlusion, even when the aorta is permanently ligated, or no lesions can be found. Juliusburger is the only author to report lesions at the end of one-half hour. Rhigetti, Jatta and Spronck, however, reported lesions only after six, twelve and twenty-four hours, respectively. One hour of temporary ligation is the minimum time required for production of lesions. Spronck, however, reported lesions after one-half hour of temporary ligation. Permanent ligation produces no changes until from three to six hours after the application, and then these resemble multiform types of cellular degeneration found in a cadaver. Concerning the duration of time of ligation necessary to produce pathologic changes, there is an astonishing discrepancy in the reports of various authors. De Buck and de Moor present the following tabulation:

Juliusburger	found changes	½ hour after ligation of 1 hour
Sarbo	found changes	1½ hours after ligation of 1 hour
Münzer and Wiener	found changes	5 hours after ligation of 1 hour
Rhigetti	found changes	6 hours after ligation of 1 hour
Jatta	found changes	12 hours after ligation of 1 hour
Spronck	found changes	24 hours after ligation of ½ hour
Jatta	found changes	after 3 hours of permanent ligation
Marinesco	found changes	after 6 hours of permanent ligation
Rhigetti	found changes	after 36 hours of permanent ligation

The nature of lesions resulting from anemia is also a controversial subject. De Buck and de Moor found that they agree with most authors on the following points: Histopathologic changes in nerve cells begin with chromatolysis, formation of a reticulum and later loss of affinity for staining. However, for a time the cell may be dark and somewhat homogeneous in its staining qualities. The cells atrophy rather than swell. The nucleus is usually more resistant than cytoplasm and does not disappear until late in the process of cellular disintegration. Marinesco alone described swelling of cells as the first change. Peripheral vacuolization emphasized by this author is found by de Buck and de Moor and others to be a rather infrequent occurrence. Jatta described central vacuolization. Sarbo described a homogeneous atrophy of the nucleus. Jatta found fragmentation of the nucleus instead. Swelling fragmentation, atrophy, fusion, etc., have all been described as pathologic changes by one author or another. Only a few observers describe

eccentric nuclei and extrusion of the nucleus from the cell. Satellitosis is only infrequently mentioned. De Buck and de Moor reported neuronophagia and a cellular infiltration, possibly of lymphocytes or some unknown wandering cells. The spinal ganglion cells are found to be resistant to anemia, but when changes occur, they are similar to those of the cells in the spinal cord. These authors concluded that there is no histopathologic picture which can be considered as pathognomic of anemia.

Hill and Mott (1900) [18] made histologic studies of brains of monkeys in which cerebral anemia had been produced by Cooper's operation. They found that in monkeys, after permanent ligation of the four main cerebral vessels, changes in cortical cells occur within ten minutes which consist of slight swelling and chromatolysis. They mentioned no controls. In animals that die within twenty-four hours, the cortical ganglion cells show diffuse staining, absence of Nissl bodies and "coagulation necrosis." When signs of recovery are evident at the end of twenty-four hours, the cortical cells of such animals are swollen, the nucleus enlarged and displaced, but with some differentiation in the chromatic and achromatic substance remaining. Mott pointed out that this indicates that only biophysical changes have taken place rather than biochemical, and therefore no permanent cessation of function of the cell has occurred. Hill and Mott, in 1906,[19] repeated these studies on cats. The material was stained by the Nissl method. They reported that in cats that die within twenty-four hours there is loss of chromatin granules and diffuse staining in cortical cells. In cats that die after twenty-four hours, swollen vacuolated cells with large eccentric nuclei occur. Cajal's stair was also used but neurofibrils showed no swelling. They concluded that large psychomotor cells of the cortex were more resistant to anemia than small pyramidal cells.

Gomez and Pike [6] studied the extensive material produced in the experiments of Stewart, Pike et al. already described under physiologic aspects. They killed these cats at various periods after termination of the occlusion of cerebral vessels and fixed the brain tissue in 96 per cent alcohol and in Muller's fluid, and stained by Nissl, Weigert and Marchi methods. They used a two-thirds grown cat for control.

They reported the following observations on this histologic material:

1. Pericellular lymph spaces are dilated two to three times the normal size. In animals allowed to completely recover, this space is reduced to normal size. In tissue taken during the period of the anemia, the spaces are reduced or not greater than normal.

18. Mott, F. W.: An Introduction to Neuropathology, Albutt and Rolleston: System of Medicine, New York, The Macmillan Company, 1910, vol. 7, p. 173. Albutt: Lancet **1**:1779, 1900; ibid. **2**:1849, 1901.

19. Hill, L., and Mott, F. W.: The Neurofibrils of the Large Ganglion Cells of Motor Cortex of Animals in Which the Four Arteries Have Been Ligatured, Proc. Physiol. Soc., London, 1906, p. 4.

2. Cats killed a short time after restoration of circulation show swollen cells.

3. It was impossible to differentiate readily between normal cells and cells of cats killed without return of circulation, or cells of animals that have recovered.

4. Cats that die many hours after restoration of circulation and following a prolonged period of anemia have cells which are shrunken and irregular in outline; pericellular lymph spaces are relatively wider than normal.

5. Two types of chromatin changes occur: The first in large pyramidal ganglion cells, where chromatin tends to be clumped and takes a diffuse blue stain; this often extends into the nucleus which loses its outline and can only be made out by the presence of deeply staining nucleolus. With more advanced changes the chromatin is broken down into fine dustlike particles and finally it may not stain at all. The second type of change occurs in small pyramidal cells and consists of loss of affinity for staining and complete disappearance.

6. In animals in which the period of anemia is long (twenty-two minutes) and the period of survival several hours, vacuolization of the cytoplasm occurs; the nucleus is displaced, but there is no evidence of extrusion from cells.

7. Occasionally the nucleus was found to take a stain similar to that taken by the cytoplasm. No change was found in the nucleolus.

8. A certain time must elapse after a period of occlusion before characteristic changes occur.

9. Neuroglia cells show no abnormalities.

10. Neurones of different animals and of different areas in the same animals show variation in susceptibility to anemia. Small pyramidal cells are the most sensitive and often show decreased affinity for staining. Purkinje's cells are next in order of sensitiveness. They show diffuse chromatolysis after thirteen minutes of anemia. The cells in the medulla are more resistant. Eight to thirteen minutes of occlusion usually produces very slight lesions. Twenty to thirty minutes produces changes not compatible with life of animals. Neuroglia cells are unaffected. The cells of the cervical cord are described as next to the medulla in their capacity to endure anemia. Spinal ganglion cells are the most resistant of all.

Cannon and Burket [2] found the following histologic changes in the cells of the myenteric plexus after three hours of anemia:

1. Disappearance of cytoplasmic granules and diffuse staining.

2. Moderate connective tissue proliferation.

3. Somewhat eccentric nuclei.

4. After three and one-half hours of anemia practically all cells have disappeared and only scattered remnants remain.

5. One and one-half hours of anemia produces no histological changes.

Tuckett (1905) [20] dissected out the superior cervical sympathetic ganglion and carefully cut off the blood supply. He reported the following changes::

1. Homogeneous staining cells with shrinkage.

2. Loss of nucleolus.

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20. Tuckett, I.: Degeneration of Nerve Cells of Rabbits Superior Cervical Sympathetic Ganglion as the Result of Interfering with Their Blood Supply, J. Physiol. **33**:77, 1905.

3. Inversion of staining—cytoplasm stains more darkly than nucleus.

4. Finally a shadow stage in which the whole cell stains poorly. If cells are well supplied with lymph they show ordinary necrotic changes seen in cadavers rather than those described above.

After periods of mild anoxemia produced by placing an animal in a low-oxygen chamber (by the technic as described in the section on physiologic aspects) Martin, Loevenhart, Bunting [17] and Ford [16] found no histologic changes.

Spielmeyer has given a great deal of study to the problem of cerebral anemia. In a summarizing paper (1928) [1] he described the usual lesions and discussed the probable mechanisms involved. With the Nissl stain he found pale areas in the cortex, due to dropping out of nerve cells. The remaining cells, when examined under high power, were seen to be shrunken, homogeneous and pale, usually corresponding well with the ischemic cell degeneration described in his book (Spielmeyer, 1922, p. 74, fig. 34).[1] This type of cell change, however, is not universal; many of the other types of degeneration may also be found. These types are classified in his book in a schematic, but useful way; he understands that histologic observation can teach little about the time element, the intensity and the specificity of the process, and warns against exaggerated interpretation. Nevertheless, the classification and the descriptions and illustrations are most helpful. The main types seen with Nissl stain are:

(*1*) Cell Swelling ("Schwellungsvorgänge," Nissl's "akute Schwellung"): The cells show rounded corners and plump processes; many of these stain blue and are visible for a long distance; the chromidial substance (Nissl bodies) is disintegrated, at least near the nucleus. The whole cell takes a diffuse blue stain, there being no unstained spaces.

(*2*) Cell Shrinkage ("einfache Schrumpfungen," Nissl's "chronischen Zellerkrankung"): The whole cell is shrunken and often elongated, including the processes. The chromidial substance stains darkly, is less in amount and may be in clumps. The spaces which normally are unstained take on color and largely disappear. The outline of the cell is angular, loses its round curves and where the processes come off there are sharp angles. The nucleus loses its roundness and may take on something the shape of the cell; it is dark and the nucleolus may be larger than normal.

(*3*) Cell Liquefaction ("Verflussigungsprozesse"): The cells are pale and swollen, with rounded outlines, the chromidial substance disappears and rings of detritus often remain in the cell body; dark-staining granules and globules are seen, most often in the processes. The nucleus is round, small and metachromatic; the nucleolus is large, dark and near the edge. This is apparently a pernicious process, and all

stages between the one described and complete disintegration are found; it was therefore called by Nissl "schwere Zellveränderung."

(*4*) Cell Coagulation ("Gerinnungsvorgange," "Koagulationsnekrose"): The cell body is pale, apparently decolorized; it is shrunken, angular and unusually elongated. The processes are lost or difficult to see; they may be encrusted with degeneration globules. No chromidial substance is seen, and the cytoplasm is almost colorless or bluish and homogeneous. The nucleus loses its rotundity and may be triangular or irregular; it is dark, often metachromatic, and the nucleolus is seen with difficulty; it is usually enlarged and at the edge. This type of change is found most frequently with vascular occlusion, and is therefore called by Spielmeyer "ischämische Zellveränderung." Subspecies of this type are characterized especially by homogeneous change and impregnation with degeneration granules.

(*5*) Alzheimer's Fibrillary Degeneration: This shows swollen, irregular cells with loss of chromidial substance, but special stains must be used, for the Nissl picture is not entirely characteristic.

(*6*) Pigment and Fat Changes: These are not well seen in Nissl stains because of the alcoholic fixation. Special stains show fat well, but these elements are normal contents of certain cells.

Buzzard and Greenfield, in their textbook "Pathology of the Nervous System" [21] (1922), summarized the accepted results of cerebral anemia as follows: Partial interference with blood supply produces cellular changes similar to those due to various poisons. Sudden and complete cutting off of blood supply from any part of the central nervous system leads to rapid cell change characterized by reduction in the size of the cell body, the whole cell staining homogeneously with the basic dye. This has been illustrated by the results of experimental ligature of the carotid and vertebral arteries or of the abdominal aorta in animals, and by the result of thrombotic lesions in human brains. There is evidence to show that chromatolysis, together with some swelling of the cell and displacement of the nucleus, may be recovered from, if and when the circulation is reestablished, but the state of cell shrinkage associated with uniform deep staining indicates that a biochemical change in the protoplasm has taken place, from which recovery is impossible.

We can conclude from this résumé of the literature that anemia, if severe and prolonged enough, produces some form of lesion of the central nervous system, that fifteen minutes or less of practically complete anemia results in permanent loss of function of many cells of the medulla and the cortex and that histopathologic changes can be made out if an animal is kept alive a certain time after the period of anemia. Some observers report changes at the end of ten minutes, but the

21. Buzzard, E. F., and Greenfield, J. G.: Pathology of the Nervous System, New York, Paul B. Hoeber, 1922, p. 13.

majority consider from one to three hours, or longer, necessary for the production of lesions. We find that almost every type of lesion has been described, but that perhaps the commonest type of cell change is the shrunken, homogeneous, dark-staining variety. Shrunken cells that have poor affinity for staining and a definite reticulum are also common. Satellitosis or glial proliferation are only infrequently mentioned. Chromatolysis is always mentioned, but apparently means different things to different observers. The variety of these observations makes it seem improbable that any type of histologic change can be described as pathognomonic. The Nissl stain seems to yield the most delicate and definite results. One is surprised in reviewing this literature by the infrequent reference to controls.

DESCRIPTION OF EXPERIMENTS

Physiologic Aspects.—No satisfactory technic for producing complete cerebral anemia, without extensive trauma to the tissues of the animal, has been devised, chiefly because of the rich anastomoses of spinal arteries with intercostals and even with vessels of the lumbar region. Consequently, we have tried several methods of cutting off the cerebral circulation:

(*1*) That described by Sherrington in "Mammalian Physiology" (1919) [22] in which the vertebrals are dissected out as they pass between the first and second cervical vertebrae; then a cord ligature is passed around the spinal column and tied firmly, thus compressing the vertebral arteries against the spine. If tied tightly enough, it shuts off the blood completely. The animal is then turned over and the carotids are exposed and clamped. This method proved unsatisfactory because in many of the cats the vertebrals gave off branches below the second cervical vertebra and it was impossible in such animals to get more than a mild degree of cerebral anemia.

(*2*) That devised by Astley Cooper and later modified and used effectively by Stewart, Pike and Guthrie et al. (1906 to 1922).[6] A midline incision is made just above the sternum, and the left subclavian and innominate arteries are dissected out to a point central to the origin of the vertebrals. Cord ligatures are then passed about these vessels in such a way that they can be quickly occluded, by pulling on these ties. This operation is rather difficult because dissection has to be done at the bottom of a hole, from 1½ to 2 inches deep. It is also difficult not to puncture the plura.

(*3*) It was found much simpler to dissect out the vertebral arteries on both sides just as they disappear around the longus colli muscle, about 1 cm. below the tubercle which forms the lowest point of attachment to the vertebral column for the scalene muscle. In this operation much less trauma is done to the tissue, and the whole experiment can be completed in half the time. In some cases, however, it was not possible by this method to produce a satisfactory cerebral anemia. When this happened the dissection was continued along the vertebrals to their

22. Sherrington, C. S.: Mammalian Physiology, Oxford, Clarendon Press, 1919, p. 147.

juncture with the left subclavian and the innominate arteries and then these vessels were ligated as in the method of Stewart and Pike. But even then a severe anemia was not produced in many cats. Stewart and Pike have recorded this as an occasional incident. Such failure can be explained by the fact (see review of the literature) that there is often a good anastomosis between intercostal vessels and the spinal arteries, which in many animals will maintain some degree of blood flow in the circle of Willis, and occasional cats may live indefinitely after permanent ligation of the innominate and subclavian arteries. Besides this anatomic difficulty it was found that unless vessels were clamped firmly, some blood would still trickle through them. Ordinary "bull-dog" clamps proved to be unreliable. With many cats, when symptoms did not appear after "bull-dog" clamps were applied, definite signs of cerebral anemia would appear at once if heavier clamps were used in their place. Usually, however, traction on cord ligatures was found to be effective in occluding these vessels. In other cases various anomalies in the anatomy of the blood vessels accounted for a failure to produce a complete anoxemia.

Young cats were used in all experiments. Light ether anesthesia was given while all vessels were being exposed and cord ligatures passed about them. Then the administration of ether was stopped and the animal allowed to come out of anesthesia to a point where it began to move a little and reflexes were present. The vessels were then occluded by traction on all ligatures; this at once produced a complete coma. In most experiments artificial respiration was given by means of a tracheal tube attached to a machine that delivered an interrupted stream of air. The rate of interruption and the amount of air were varied according to the circulatory needs of the animal.

As already noted, the technic used in these experiments does not produce a complete or accurately calculable amount of cerebral anemia. Therefore, the signs and symptoms had to be used as a measure of the severity of the anemia. In our series of experiments we have attempted to subject cats to as long a period of anemia as was compatible with a degree of recovery sufficient to enable them to live for several days after the experiment. In practice this proved a delicate and difficult matter. Of ninety cats, only twenty survived longer than twenty-four hours. In the majority of the other animals, even when artificial respiration was kept up for two hours after the period of the occlusion of the vessels and the heart continued to function satisfactorily, normal respiration never returned. In another group (fifteen) the respiratory center recovered, but the animals developed a series of convulsions and died. There were also cats in which respiration would reappear and function fairly well for an hour or more only to become irregular or rapid and then cease entirely.

After observing the severity and the remote effects of various symptoms that appeared during the occlusion period in a number of cats, we found two symptoms to constitute the most reliable criterion of severe anemia: (*1*) cessation of respiration within from one to two minutes after occlusion of the vessels; (*2*) the appearance of convulsion during the occlusion period. Unfortunately, convulsions frequently meant that the anemia had produced such damage that the animal would not survive for more than a few minutes or hours, even when the cerebral circulation was restored immediately after their appearance. Other symptoms that appeared during the time the cerebral circulation was cut off were found to be unreliable as indications that severe anemia has been produced. There were, of course, exceptions to these rules. Some animals never developed convulsions even during long periods of occlusion and yet subsequently could not be resuscitated because of severe damage to the respiratory center, while others in

which respiration returned developed convulsions, marked extensor rigidity and extreme stupidity. Most observers, including Stewart and Pike, have not mentioned convulsions as occurring during the period in which cerebral vessels were occluded. Yet they have obviously subjected animals to as prolonged periods of relatively complete cerebral anemia as we have obtained in our animals. The only way we have been able to account for this discrepancy in observations is the fact that their cats were probably under rather deep ether anesthesia during the occlusion period. We have found that if we failed to allow animals to come out of ether until the corneal reflexes had returned and some involuntary movements had appeared, no convulsions would develop even when the anemia was sufficiently severe to damage the respiratory center permanently and result eventually in the death of the animal. In other respects we have been able to confirm the observations of former investigators as to the immediate effects of cerebral anemia.

The results of a satisfactory occlusion of cerebral vessels observed in our cats may be summarized as follows: The mucous membranes of the mouth and nose immediately become pale. The animal stiffens out, then becomes limp and the reflexes usually disappear. At the same time, the pulse rate increases, and respiration labors, then becomes irregular and gasping and finally ceases, at the end of from one to two minutes. With cessation of respiration the heart slows down, only to become rapid again from two to four minutes later as the vagus center fails. If one looks at arteries of the retina during this period, one can see them decrease in diameter. As the blood flow slows down, one can make out the red corpuscles passing through smaller vessels (we have never observed the blood flow to cease entirely except in animals in which the heart had stopped). Thus, we soon have an animal that is completely relaxed, usually with all reflexes absent (occasionally there are exceptions), dilated pupils, no tear secretions, depressed, furrowed cornea and pallid mucous membranes in the nose and mouth. The heart is slow and the pulse is usually weak in spite of adequate artificial respiration. If the anemia is severe and sufficiently prolonged, convulsions usually appear. They may be preceded by clonic movements of one foot or by rigidity of the whole body. Then there is a brief period of tetanic convulsions which is quickly followed by gross clonic convulsions, often involving the whole body. The first seizure may be mild and last only a few seconds, but if cerebral circulation is not restored at once, others quickly follow and they become so violent that it is often impossible to keep the cannula which maintains artificial respiration in the trachea. The usual outcome of such severe convulsions is death. In some animals convulsions never appear. In our series of ninety cats convulsions occurred in sixty-five during the occlusion period.

When the vessels are released and the cerebral circulation is restored, the mucous membranes immediately become pink. Respiration usually returns within from fifteen minutes to one hour if it is to return at all. The corneal and the other eye reflexes appear about the same time as

the swallowing reflexes; the deep reflexes follow within from four to eight minutes. It must be noted, however, that there is great variation as to the disappearance and return of reflexes. This is especially true of the corneal reflex. We have been unable to explain the variability in these observations.

Shortly after the circulation was restored, the majority of animals developed extensor rigidity of the fore legs, which occasionally persisted for as long as one hour. Most of the cats recovered consciousness and attempted to walk within thirty minutes; others in from three to four hours. A smaller group had no convulsions until the second or third day. Of these, four died apparently of respiratory failure during the convulsions, which were frequent and severe. Many of these animals were observed to have from two to eight seizures. The ones that died usually developed "status epilepticus," an almost continuous series of convulsions, before death.

A prominent feature that has not been emphasized by other observers was the failure of practically all of the cats to recover their preoperative intelligence. These animals appeared lethargic and showed no normal interest in their surroundings. When paws or tail were pinched, they snarled or yowled a little, but made no attempt to ward off or localize the injury. When left alone they slept with their head buried in a corner of the cage. Many animals did not seem to know enough to eat the food placed in front of them, but would swallow when fed with a spoon. We concluded that this loss of normal intelligence was an indication of severe disturbance in cortical function. Many other forms of abnormal behavior were less frequently observed. Five animals, instead of having ordinary clonic convulsions, developed violent and aimless running and climbing spells; they would persist in these movements even when their heads were jammed into a corner between the side and roof of the cage. They might hang in such a position until completely exhausted. Three died in this type of attack, apparently from exhaustion. Two animals developed extremely rapid respiration, but only slight and occasional convulsions. They died of respiratory failure within twelve hours. None of our animals developed paralysis, blindness or areas of anesthesia that we were able to make out. The occlusion period required to produce convulsions or permanent impairment of the respiratory center was extremely variable, but as has been emphasized in our review of the literature, the presence of arterial anastomoses makes the production of complete anemia impossible with the technic employed; such variations are to be expected. The minimum length of the occlusion period was two minutes; the minimum period, twenty-four minutes. Only four of the animals approximated complete return to the preoperative condition even after from five to ten days.

Furthermore, twenty cats after periods of anemia of five minutes developed a series of severe convulsions that ended in death. When it is considered that we did not produce complete anemia, one can conclude only that cortical cells probably are not capable of enduring a complete anemia for as much as ten minutes and that this is probably a liberal estimate. The records of other observers, of recovery after longer periods of anemia, can readily be explained by failure of these workers to produce complete cerebral anemia.

Histopathology.—Of the series of ninety cats subjected to periods of anemia, thirty-two were selected for histopathologic study.

Of these, all but four showed unquestionable signs of severe cortical disturbance such as convulsions, extensor rigidity or marked and persistent stupidity. All animals, except seven that died in the midst of severe convulsions and were chosen for that reason, were lightly anesthetized with ether and killed by injection into the carotid artery, of 30 cc. of neutralized 10 per cent commercial formaldehyde solution. The brains were then immediately removed. One hemisphere was placed intact in a jar of 10 per cent commercial formaldehyde. Of the other hemispheres, two small sections were cut from the frontal, parietal and occipital lobes, respectively. One set was fixed in 80 per cent alcohol for paraffin embedding and staining with cresyl violet; the other in 10 per cent commercial formaldehyde for frozen sections and staining with scharlach R. The intact hemispheres were used to make large celloidin sections for localization of the lesions. Two days after being placed in formaldehyde, they were cut into serial blocks approximately 6 mm. thick. These were then embedded in celloidin, and the third or fourth section from each anterior surface of each block was stained with cresyl violet. In thirteen cats, selected as representative, a third block was cut from each frontal, parietal and occipital region and stained for oligodendroglia. Del Rio Hortega's silver carbonate method, as modified by Penfield,[23] was used.

For control, five not quite full-grown cats were lightly anesthetized with ether and killed by the injection of 10 per cent commercial formaldehyde in exactly the same manner as described for experimental animals.

Description of Lesions.—In all cats that developed symptoms of marked cerebral anemia some sort of lesions were found in the cerebral cortex. These changes proved to be varied in type and to be difficult to correlate with the survival time, the length of time after operation at which the cat was killed, with the duration of anemia, or with the severity of the symptoms which the cats displayed. We have compiled a table which correlates important symptoms observed in each animal, during and after the anemic period, with the lesions subsequently found in the cerebral cortex. The symptoms listed in the table are self-explanatory, and their importance and relationship to cerebral anemia have already been discussed. The headings used to describe important

23. Penfield, W.: Oligodendroglia and Its Relation to Classical Neuroglia, Brain **47**:430, 1924. Penfield, W., and Cone, W.: Acute Regressive Changes of Neuroglia, J. f. Psychol. u. Neurol. **34**:204, 1926.

Observations on Cats that Died at Various Periods After the Termination of the Occlusion Period

Cat	Duration of Life After Experiment	Length of Occlusion Period	Convulsions During Occlusion Period	Convulsions After Occlusion Period	Extensor Rigidity	Stupid	Satellitosis	Shrunken Homogeneous Nerve Cells	Swollen Nerve Cells	Vacuoles in Nerve Cells	Cells with Spike-Like Processes	Areas of Devastation	Areas of Round Cell Infiltration	Fat in Perivascular Spaces	Fat in Nerve Cells	Cat
Cats That Died Within One Hour of End of Occlusion Period																
5	2 minutes	2 minutes	+++	0	0	..	+	+	0	0	++	0	0	0	0	5
11	0 minutes	17 minutes	Whole animal rigid	—	+	..	+	++	0	0	+	+	0	+	0	11
13*	13 minutes	2 minutes	++	—	0	..	++	+++	0	0	+	++	++	0	0	13*
19	60 minutes	20 minutes	+	+++	+	..	+	+++	0	0	++	+	+	++	+++	19
22	50 minutes	7 minutes	+++	+++	-	..	..	++	0	0	++	0	0	+	++	22
24	25 minutes	7 minutes	+	+++	0	..	..	+++	0	+	++	+	0	+	0	24
26	45 minutes	4 minutes	++	++	0	..	0	++	++	0	++	0	0	+	++	26
33†							0	+	0	0	0	0	0	+	0	33†
Cats Killed 1 to 4 Hours After Termination of Occlusion Period																
10*	4 hours	15 minutes	+	+++	++	+	++	+	0	+	0	+	++	+	0	10*
15	2 hours	24 minutes	0	++	+	0	+	+	+	0	0	0	0	+	0	15
Cats Killed 20 to 24 Hours After Termination of Occlusion Period																
3	24 hours	23 minutes	0	0	0	+	+	+	0	0	0	0	0	+	0	3
18	22 hours	5 minutes	++	0	0	+	+	++	0	0	++	+	0	+	0	18
25	23 hours	6 minutes	0	++	++	++	0	++	0	0	+	+	0	+	0	25
34	20 hours	12 minutes	0 Ether	++	+++	++	+	++	++	++	+++	0	0	++	0	34
Cats Killed 1 to 2 Days After Termination of Occlusion Period																
1	45 hours	8 minutes	+	0	0	++	+	++	+	0	0	0	0	+	0	1
2	45 minutes	7 min. and 21 min.	++	+	+	++	+	+++	0	0	0	0	0	++	++	2
14	28 hours	10 minutes	++	+++	++	++	++	++	+	0	0	++	0	+	+	14
16	36 hours	3 min. and 3 min.	+	0	0	0	+	+	0	0	0	0	0	++	0	16
23	25 hours	6 minutes	+++	+++	+++	+++	+	+++	+	+	0	+++	0	++	+	23
35	48 hours	5 min. and 5 min.	+++	+++	+	+++	+	+	++	++	0	0	0	+++	+	35
20	50 hours	17 minutes	+	+++	++	++	0	++	++	+	0	+	0	++	+	20
Cats Killed 3 to 5 Days After Termination of Occlusion Period																
32	3½ days	4 minutes	++	+++	+++	+	+	+++	0	++	0	+	0	++	+	32
12	4 days	15 minutes	0	0	++	++	+	+++	0	0	0	++	0	+	0	12
6	3 days	20 minutes	++	0	0	+	0	++	0	0	0	+	0	+	+	6
21	4 days	13 minutes	0	++	+	+++	+	++	+	+	0	+	0	+	0	21
8	3 days	24 minutes	++	+	0	++	+	+	+	+	0	+	0	+	+	8
28	4 days	8 minutes	+	++	+++	+++	0	++	0	0	0	+	0	+	+	28
29*	5 days	6 minutes	0	0	0	++	0	++	0	0	0	+	0	++	+	29*
31	5 days	5 minutes	0	+	+++	++	+++	++	+	+	0	++	+++	+	++	31
Cats Killed 11 to 16 Days After Termination of Occlusion Period																
4	11 days	20 minutes	++	+	++	+++	+++	++	+	+	0	0	0	+	+	4
27	16 days	5 minutes	0	0	+	+++	0	++	+	0	0	+	0	++	+	27

* Cats with evidence of some form of encephalitis.
† Died from too much ether just as vessels were exposed.

lesions will be explained in the following summary of the histopathologic observations:

Areas of Devastation.—The most severe lesions were found in animals that had had convulsions and that had lived at least twenty-four hours after the termination of the period of cerebral anemia. Low power microscopic examination of the cortex of these animals reveals small scattered areas of necrosis where many cells have disappeared and those remaining are abnormal. These areas interrupt the normal orderly laminations. We have called these holes in the cortex "areas of devastation." They correspond to Spielmeyer's "Herde" in man. These areas occur only in animals that survived more than twenty-four hours, and even among these only three have large and frequent areas of devastation. Animals in which small ill defined areas of devastation are present are tabulated as +; cat 23, in which the lesions are most severe and a few others approximately as severe, are graded +++. An intermediate group is indicated by ++. The striking thing is the loss of nerve cells, the glial and vascular tissue being, if anything, hypertrophied in these areas. At the center of such a focus is found necrotic material, unidentifiable débris, and often parts of nerve cells large enough to recognize; usually these appear to be nuclei, pale and without limiting membrane. If a nerve cell survives near the center of a devastated area, it is always abnormal, usually pyknotic with granules and globules along its only remaining dendrite; the nucleus may be so dark that the nucleolus is scarcely discernible. Near the edge of the devastated area such nerve cells are abundant (various types of nerve cell degeneration are described later) and swollen nerve cells are often found; in fact the degeneration may be severe or mild and of various types. Characteristically, the nerve cells become shrunken and homogeneous closely resembling Spielmeyer's ischemic nerve cell change. Throughout the devastated area there are numerous glia nuclei; these are apparently increased in number; in some cases the oligodendroglia cells are conspicuously increased, often acting as satellites to the degenerating nerve cells. Special stains, however, show no acute swelling of the oligodendroglia cells. The capillary walls become somewhat more conspicuous than usual, and in some foci it seems that capillaries are increased in number considering the area observed. Microglia occasionally are common along the small vessels. Almost invariably these areas of devastation are located in the third and fourth laminae of the cortex. Often they spread into the fifth lamina. Small foci are usually round, but larger ones invade the laminae in such a way as to look oval or even like stripes of necrosis when observed in sections 20 microns thick.

The other lesions observed are much more diffuse in character and therefore more difficult to evaluate. Such lesions consist for the most part of scattered ill defined areas where there are many more abnormal cells than in any part of the cortex of control cats. The cells of lamina V are most frequently abnormal, but cells of other laminae are so commonly injured that it is impossible to lay much stress on this observation. Furthermore, although the large and small pyramidal cells are apparently most subject to this type of lesion, it is so much easier to see the abnormalities in them than in smaller nerve cells that we cannot be confident of the conclusion that lamina V is really more vulnerable than III, IV and VI. Obviously I and II are usually spared (figs. 1 and 2).

Shrunken Homogeneous Cells.—Although a variety of types of cellular disintegration can be found in these anemic brains, the cell most characteristic of such lesions seems to be shrunken and darkly staining. The shrinking causes concave depressions in the sides of the cell and angular corners at the points where the

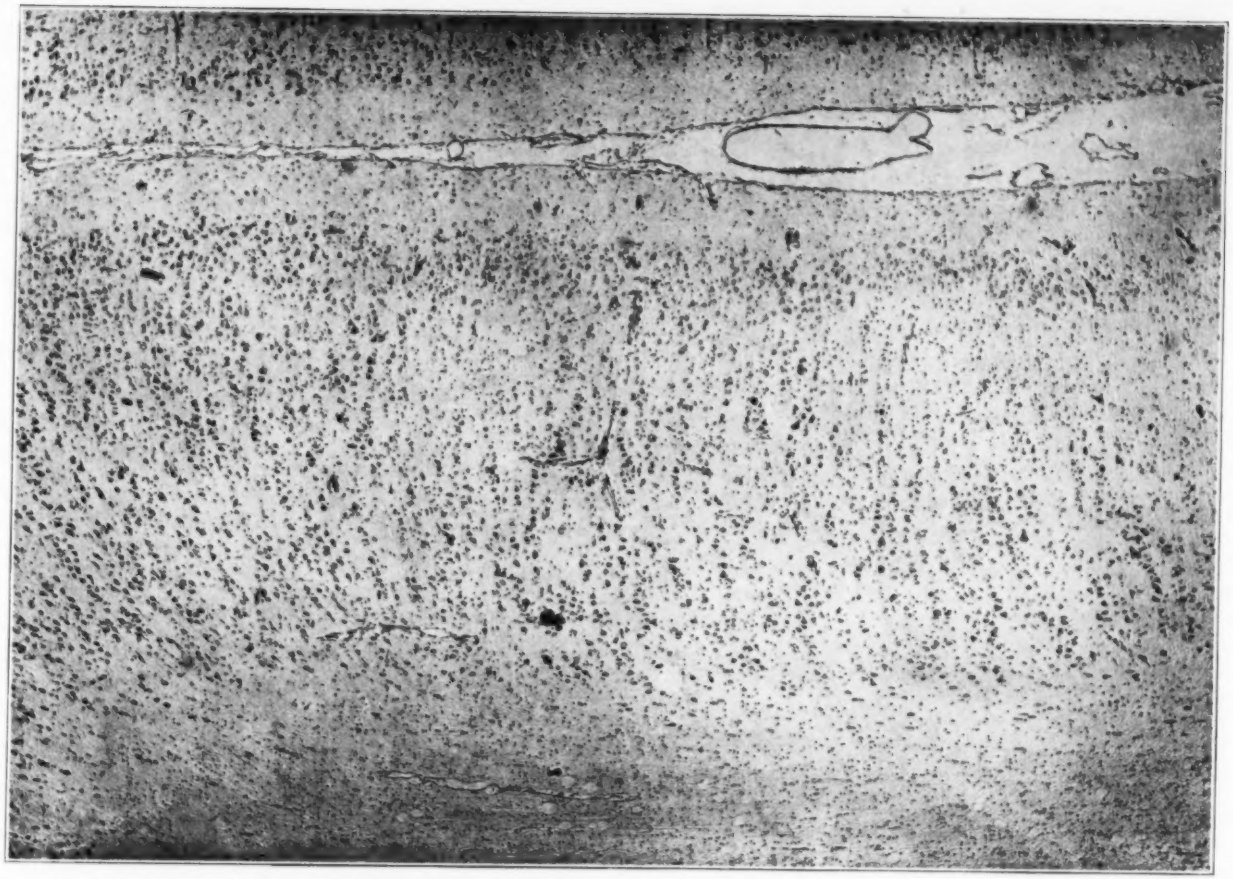

Fig. 1.—Area of devastation in the frontal cortex of a cat with acute anemia for six minutes, living after the operation for twenty-four hours. Laminae I and II of the cortex are practically normal. The lesions lie largely in laminae III, IV and V. These devastated areas are easily recognized by their loss of nerve cells and by the persistence of the glia and mesal dermal elements (cat 23; low power photomicrograph; cresyl violet stain.

processes extrude (fig. 3). The cell itself loses in diameter but not in length; often it seems to be even prolonged. The dendrites and axon can be seen for a long distance, often they are wavy or crinkled; occasionally small globules of dark-staining material are seen in the processes, but as a rule they are pale violet (with the cresyl violet stain). The dark-staining mass of the cell stops abruptly at the base of the process. The nucleus is of irregular shape, often taking on the shape of the part of the cell in which it lies, as if the shrinking cell wall pressed on its nucleus. More often the outlines of the nucleus cannot be made out clearly or perhaps not at all. It stains darkly like the rest of the cell, but is often more

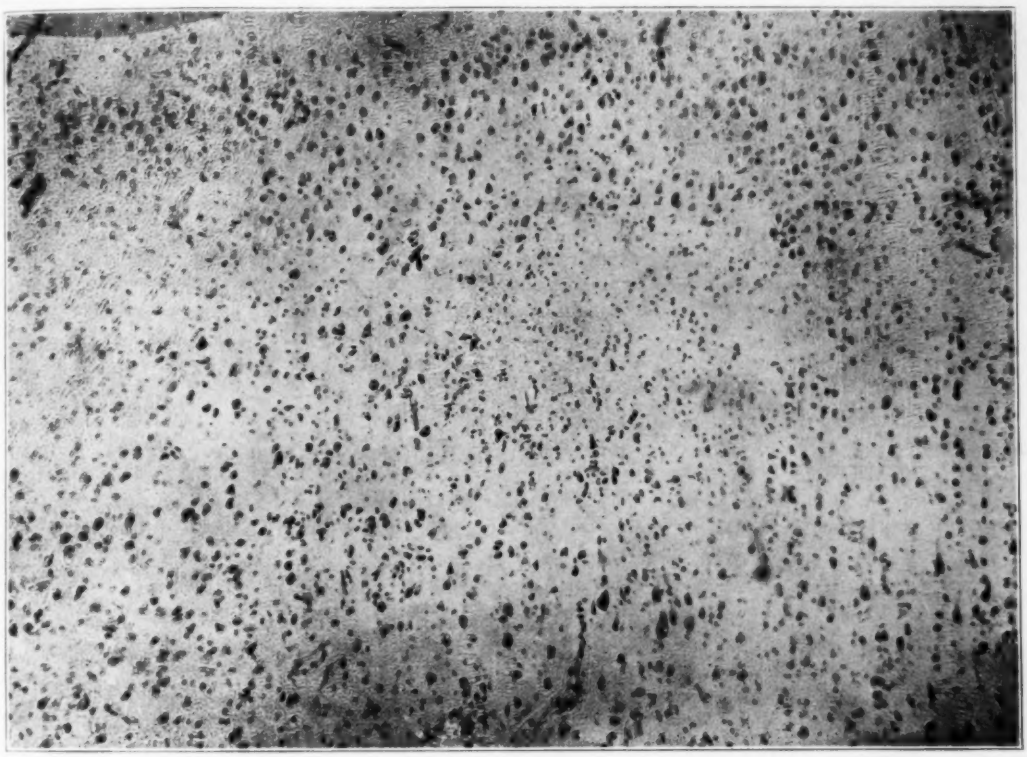

Fig. 2.—Higher magnification of the areas of devastation from the same specimen as that illustrated in figure 1.

metachromatic with refractile streaks. The best criterion of the presence of the nucleus, however, is the visibility of the nucleolus, which usually persists as a round and dark body (fig. 4) until the cell has become so dark and hemogeneous that no structure can be made out (fig. 5). The cytoplasm in general is dark purple, with pink refractile lights; the darker masses are both along the periphery and near the nucleus, obscuring the nuclear outline, but accenting the cell margins. In very much shrunken cells the cytoplasm is almost uniformly dark purple, homogeneous and glassy in appearance. Occasionally, the nucleus is eccentrically placed or may be entirely gone. Vacuoles are rare in this type of

cell. The end stage of this process seems to be fragmentation and disintegration into dark, dustlike particles.

Cells with Spikelike Processes.—In all animals that died in convulsions within an hour after the arterial occlusion period, a special type of cell change seems to form the characteristic lesion. In these cells there is a tendency to dark staining and homogeneous appearance; the processes stick out like icicles, and can be followed for an unusually long distance. We have called them cells with "spikelike processes." Often the processes are seen in the intercellular tissue, lying alone without attachment to a cell. Usually they are pale violet, sometimes almost colorless, but they characteristically come off from the cells at an acute angle, look darker and longer than normal and seem to end sharply "like icicles" (figs. 6 and 7). They do not occur with any frequency in animals that lived more than twenty-four hours after the end of the anemic period, and they are rare in control animals.

Swollen Cells.—In a few animals many cells are swollen, and in cats 34 and 35, especially, they are more numerous than the shrunken homogeneous variety. In these cells the swelling results in loss of normal angles, the cytoplasm becomes light staining, and chromidial substance is displaced to the periphery or disappears entirely. Some of these cells are pale; the processes are not clear or may be swollen. Occasionally, vacuoles appear; the nucleus may become eccentrically placed and may even be extruded from the cell. A few such cells appear only as faint shadows. Contrary to the observations of Mott and Hill, that swollen cells are an indication of acute anemia of the cortex, we have found that this type of cell is infrequent in animals that have lived less than forty-eight hours (fig. 8) after the anemic period, and common in cats that lived from three to eleven days. Furthermore, in cat 35, that died in convulsions on the third day, swollen cells are more numerous than in any other animal, and form the characteristic lesion (fig. 9).

Vacuolated Cells.—Except in the few cats in which swollen cells are common, vacuoles within cells are infrequent and not characteristic of the lesions.

Satellitosis.—Although, in all animals in which lesions are marked, there is an increase in the number of satellite cells and evidence of phagocytosis, (figs. 2 and 3) there are many cats with slight but definite lesions that do not have a demonstrable increase in satellites over the control animals.

Areas of Round Cell Infiltration.—Scattered throughout the cortex of cats 10, 13, 29 and 31 are nests of small round cells. The meninges and perivascular spaces also show some infiltration with lymphocytes and possibly glia cells. Along with these lesions there are also areas of devastation and numerous shrunken homogeneous cells. We have included these animals for the sake of completeness, but consider the cell nests and perivascular infiltration to be the result of an intercurrent infectious encephalitis, and not of cerebral anemia.

Perivascular Spaces.—In all but four experimental cats, the perivascular spaces and perineural spaces are wider than in four of the control animals. One control has spaces that are almost as wide as those in some of the cats subjected to anemia. There is no evidence that spaces are wide in cats that died shortly after the period of anemia, or that they decrease in size as the animal recovers. Cat 27, that lived sixteen days after the period of anemia, has spaces as large as those in many of the animals with an acute condition.

There is a possibility that variations in the technic of fixation, embedding and staining may widen or shrink perineural and perivascular spaces; this makes the observations as to the relative size of these spaces in this type of material unre-

Figure 3

Figure 4

Fig. 3.—Water color drawing by one of the authors (S. C.) of an early stage of a shrunken homogeneous cell in which the outlines of the nucleus and the nucleolus are lost. The processes of the cell are long and conspicuous and leave this cell body at acute angles. This is from an animal that underwent anemia for seventeen minutes and thereafter lived for fifty hours (cresyl violet stain; cat 20; line ruled on margin indicates length of 50 microns).

Fig. 4.—Another example of the shrunken homogeneous cell with dark staining cytoplasm and a glassy refractile appearance. The nucleolus still persists, although the outline of the nucleus is lost. The processes are long and conspicuous and have some small dots of production of degeneration. There are four glia satellites (cresyl violet stain; cat 20).

Figure 5

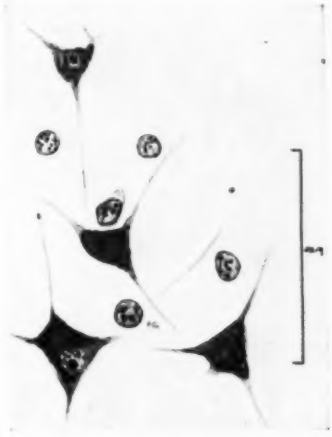

Figure 6

Fig. 5.—Another example of the shrunken homogeneous cell. This shows the common extreme shrinkage with nucleus and nucleolus lost and great elongation of the cell body. The cytoplasm is dark and homogeneous. A few globules of degeneration products are visible at the periphery (cresyl violet stain; cat 20).

Fig. 6.—Cells showing area of degeneration with the conspicuous spikelike processes. Here various stages are shown, the nucleolus being always observable though sometimes obscured. The nucleus has largely lost its membrane. The cytoplasm has become more or less homogeneous and stains darkly. There are numerous glia satellites. These cells are from the brain of an animal which underwent an acute anemia for seven minutes and thereafter lived for only fifty minutes (cresyl violet stain; cat 22; cells from lamina III of the cortex).

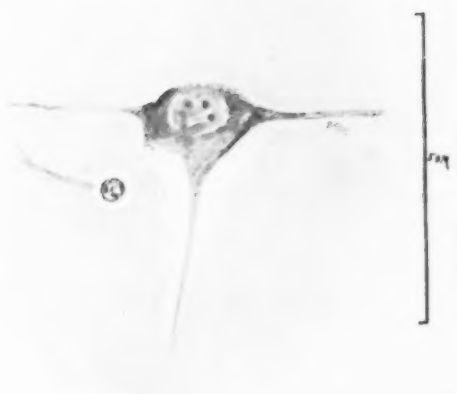

Fig. 7.—Another example of a cell with spikelike processes but with pale cytoplasm and an appearance more corresponding with Spielmeyer's "Ischemic change." Here the cytoplasm has become coagulated but does not show the dark staining reaction. This specimen is from a cat which underwent four minutes of acute anemia and thereafter lived for only forty-five minutes (cresyl violet stain; cell from lamina III of the cortex; cat 26).

liable and consequently of little value. We are unable to confirm the observations of Gomez and Pike that, in animals killed shortly after the restoration of circulation, the perineural spaces are increased in size, and that they tend to return to normal dimensions in cats which have been allowed a certain period to recover.

Fat in Nerve Cells.—Only a few cats show an unquestionable deposit of fat in cortical nerve cells, when stained with scharlach R. In the majority of the other animals a few fine reddish-staining droplets in the cells can be made out,

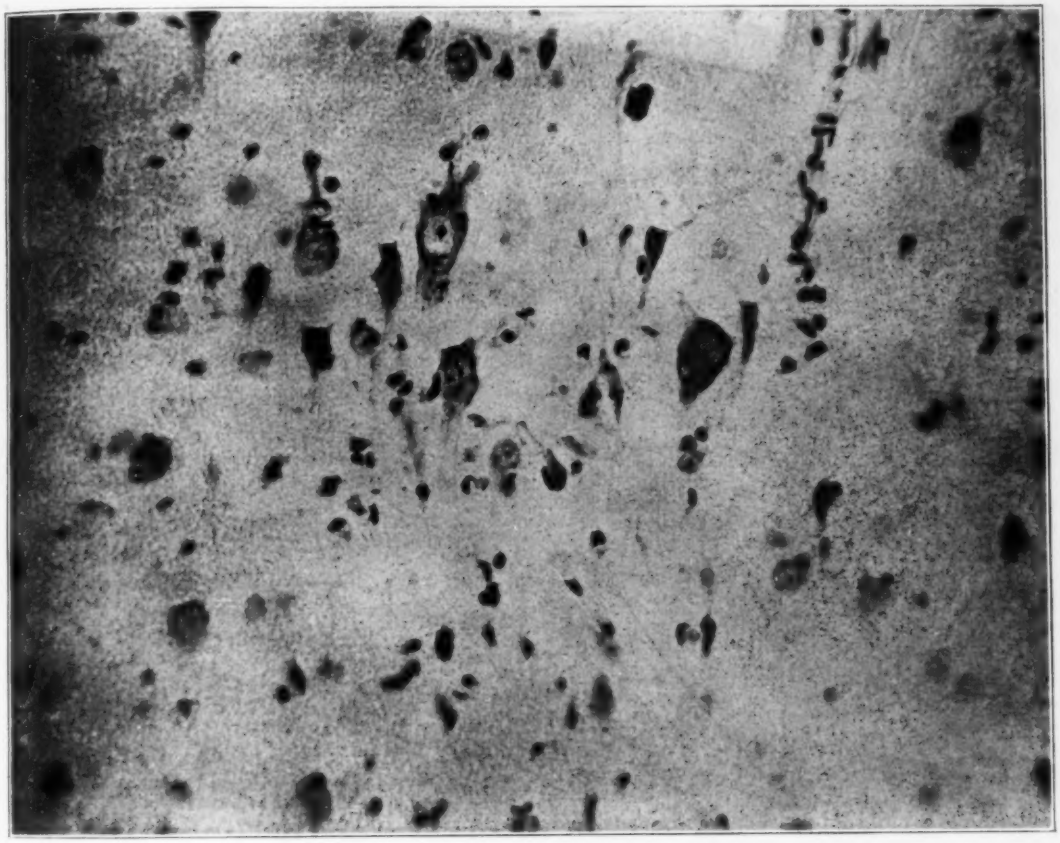

Fig. 8.—Photomicrograph of swollen cells of the cortex of a cat which underwent anemia for six minutes and thereafter lived for twenty-five hours (cresyl violet stain; cat 23).

but their importance as indicators of cell abnormality is questionable. The perivascular spaces have considerable quantities of red-staining fat in them. This usually lies in the endothelial cells (fig. 10). Little is present in control animals. The amount, however, does not correlate definitely with other pathologic changes.

Vessels.—In only three animals are the vessels at all abnormal. In these the walls are slightly thickened, and the vessels appear to be increased in number.

perhaps because they are conspicuous. The vessels of animals that died in the midst of convulsions are definitely dilated and congested with blood.

Meninges.—Two cats have slightly thickened meninges.

Glia Cells.—A definite increase in the number of glia cells was seen in only two animals, if we except satillitosis by oligodendroglia cells (which has been discussed already in describing the nerve cells). These two animals seemed to have a diffuse increase in oligodendroglia nuclei throughout the cortex. Microglia were seen occasionally near blood vessels, especially in the devastated areas.

Oligodendroglia cells were studied especially in thirteen representative cats [24] (as described under "technic"). Although these animals had severe lesions and severe symptoms, no abnormality of the oligodendroglia cells could be found.

Comparing our observations with those of other investigators, we find ourselves in closest agreement with Spielmeyer. Our shrunken and homogeneous cells resemble his ischemic change, the cell coagulation, but we find it difficult to differentiate between this and the simple cell shrinkage of Nissl. In short, the commonest abnormality of the nerve cells found by us is a combination of the simple cell shrinkage and cell coagulation; both types occur in close proximity in our anemic lesions and intermediate stages are at present difficult to refer to one or the other class with any definiteness. The "cells with spikelike processes" are a case in point. Here, there is evidence within the cell body of early coagulation, but the obvious change is in the conspicuousness and sharpness of the dendrites of the cells, giving the nerve cells a prickly appearance. The pale cells described by Spielmeyer were rare in our experience as compared to the abundant dark-staining cells.

Since we worked with controls it has been possible to throw some light on the time element. It was found that the shrunken and homogeneous appearance may develop in a few minutes; we believe that this is not a chronic change, as held by Nissl. On the other hand, the swollen nerve cells, though not uncommon in many animals, were usually found in more chronic lesions. This again is in disagreement with Nissl and with Mott who state that the swollen cell is an acute phenomenon.

The severe degenerative changes described by Spielmeyer as cell liquefaction were never seen in these animals. Fat changes were occasionally seen, especially in those animals which lived a long time after the cerebral anemia, but the fat globules were small and much less conspicuous than those seen in cerebral infarcts in man. Fat in the perivascular spaces or in the endothelial cells of small vessels was an almost universal observation after cerebral anemia, whereas the control animals showed little fat in this location.

Although these cell changes when described and illustrated seem definite, it has been only with great pains and constant checking of lesions by comparison with normal animals that a standard for "abnor-

24. We are indebted to Mr. W. P. Reed for this special work.

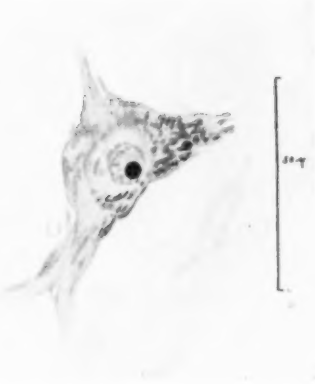

Fig. 9.—Swollen cell from lamina V of the parietal lobe of a cat which underwent anemia for two periods of five minutes each and thereafter lived for forty-eight hours. This cell shows the "acute swelling" described by Nissl, but in our experience found usually in the more chronic lesions. Note the dark nucleolus, the loss of the nuclear outline, the rounded convex curves of the cell body and the thick processes. The chromidial substance is pale and largely distributed in the periphery of the cell (cresyl violet stain; cat 35; parietal lobe of lamina V).

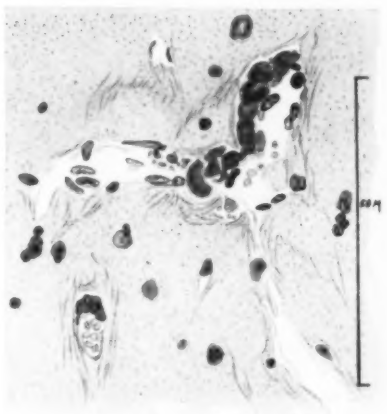

Fig. 10.—Drawing of a small blood vessel with its perivascular space which contains many fat globules which stain with "ponceau fett." In the small blood vessels in the lower left hand corner, the globules of fat appear to lie within an endothelial cell. This is also true of some of the globules in the larger vessel, but it is often difficult to determine whether this abnormal fat lies freely within the perivascular space or is inclosed in the endothelial cell. The specimen is from an animal which underwent anemia for a period of twenty minutes and thereafter survived for sixty minutes. Control animals show only small amounts of fat in the perivascular spaces.

mality" has been decided on. The subjective element is surprisingly great. It is all too easy to look through a microscope and focus one's attention on the few abnormal cells in a normal control animal. To keep the normal constantly in mind and to satisfy ourselves of our accuracy it was frequently necessary to test each other with unknown abnormal and normal slides. The gradations between "normal" and "ischemic" cortex are many and subtle. Only the striking lesions, such as the areas of devastation, could be quickly and surely recognized. Consequently, in the study of such disturbances as these a more specific and refined method must be developed if one is to obtain profitable histologic observations.

SUMMARY

Acute cerebral anemia is a common occurrence in certain industrial accidents, such as electric shock and carbon monoxide poisoning, and perhaps in many medical conditions. Spielmeyer has described lesions in the cerebral cortex which he considers to be due to vascular spasm. Similar lesions have been produced by us in these experiments, by ligaturing the blood supply to the cerebrum for a period of ten minutes. Many other investigators have made similar experiments, but most of them have not realized the richness of anastomosis between the arteries of the brain; thus they have been led to believe that they had caused complete anemia of the brain when such was probably not the case. The anatomic variations are so numerous that one must rely on the symptoms produced to indicate whether or not a severe anemia has taken place. The two most reliable were: cessation of respiration a minute or two after ligaturing the arteries, and the appearance of convulsions during or after the period of arterial occlusion. When these symptoms occurred, lesions were usually found in the cortex, especially in those animals that survived for several days. If the animal died within a few minutes, the only microscopic changes usually found in the cortex were shrinkage of the nerve cells and homogeneity of the protoplasm, the dendrites becoming conspicuous and spikelike; whereas if the animal survived for three days or longer, areas of devastation were commonly found in the cortex. These small areas resemble closely the lesions described by Spielmeyer as ischemic foci.

The difficulty was to cause in the animals an anemia severe enough to develop these lesions, and then keep the animal alive. Of the ninety cats operated on by us, only twenty survived for twenty-four hours or more. Failure of normal respiration to return was the commonest cause of death; convulsions also caused many deaths. Unlike some investigators, convulsions in our cats usually occurred during the period of occlusion as well as later, after the blood was allowed to return to the cortex;

this may be explained by the fact that light ether anesthesia was given and the animals were allowed almost to regain consciousness before the arteries were ligated. Another interesting observation was that all the cats which lived long enough after the anemia to recover from the ether and shock showed pronounced stupidity; they reacted more sluggishly and less intelligently than before the operation.

A table of the symptoms observed and lesions found in thirty-one cats has been compiled. Microscopically, the following abnormalities were commonly found: Satellitosis was observed about the nerve cells in twenty-one of the thirty-one; its degree of severity seemed to bear no relationship to the symptoms or duration of life of the animal. Shrunken homogeneous nerve cells were found in every case, but the degree of shrinkage was just as severe in those animals that died acutely as in those that survived for several days. In general, those animals that had early and severe convulsions had the more marked lesions of this type in the nerve cells. Swollen nerve cells were found in only thirteen of the thirty-one cats, and eleven of these observations were in the more chronic lesions. Vacuoles in the nerve cells were found in only eleven cases, and these also were usually the chronic ones. Cells with spikelike processes, however, were found in ten of fourteen of the animals that died acutely, and not at all in the seventeen animals that survived forty-five hours or more. Areas of devastation were the most obvious lesions in the eight animals that survived from three and one-half to five days; in the other twenty-three animals they were found eleven times. Fat in the perivascular spaces was found in all twenty-eight animals that survived more than thirteen minutes. Fat in the nerve cells occurred in sixteen of the twenty-eight that showed fat in the perivascular spaces. The fat globules were usually small and not bright red; they were found most consistently in those cases that survived more than three days (eight of ten cases). The blood vessels, meninges and glia cells showed only insignificant changes. The cell changes described seem definite, but so subtle are the gradations between "normal" and "abnormal" that it was necessary constantly to compare the slides with normal control specimens. A new method for determining the effects of anoxemia is greatly needed.

CONCLUSIONS

1. Cerebral anemia, if sufficiently complete and prolonged, produces lesions that are demonstrable in sections of the cortex stained by Nissl's cresyl violet method.

2. No one type of lesion can be said to be pathognomonic of cerebral anemia.

3. The most severe lesions consist in focal areas of necrosis.

4. Shrunken homogeneous and dark-staining cells predominate in the lesions of the majority of the cats, but swollen vacuolated cells are not infrequent.

5. Focal areas of necrosis require at least twenty-four hours to appear, but shrinkage, chromatolysis, and homogeneous-staining of the cells appear immediately after a period of cerebral anemia which is sufficiently complete and prolonged to cause death.

6. The size of perineural spaces does not seem to depend on severity of anemia, or on the length of time the animal lived after the period of anemia.

7. Lesions are usually diffuse, but the most marked changes occur in laminae III and V.

8. Large and small pyramidal cells appear more susceptible than other cerebral cells.

9. Oligodendroglia cells show little or no swelling even in cats in which most of the nerve cells are abnormal.

Owing to the fact that previous investigators have not stressed the importance of spinal arteries in maintaining some cerebral circulation after all other vessels have been tied, the capacity of cerebral cells to endure cerebral anemia has been overestimated. Our experience indicates that periods of anemia of not more than ten minutes result in permanent injury to the cortex, and not uncommonly in changes which end in death from convulsions or failure of the respiratory center. The occasional recovery of cats after an anemic period of fifteen minutes can readily be accounted for by the presence of unusually good anastomosis. Therefore, ten minutes of cerebral anemia is sufficient to impair cortical cells permanently. Even this figure may be high, because it is not probable that a complete, cerebral anemia was produced in any of the animals.

PROTOCOLS

Condensed protocols are included to illustrate the nature of the experiment and the symptoms displayed.

CAT 2.—3 p. m., etherized; vessels exposed; 4:30, carotid and vertebral arteries occluded; respiration only temporarily slowed; retinal vessels showed little evidence of anemia; 4:37, vessels released; innominate and left subclavian arteries exposed; 5:03, vessels occluded for second time. Respirations stopped; retinal vessels this time became small and corpuscles were seen flowing through; 5:17, tonic and clonic convulsions of whole body lasting thirty seconds; 5:19, second convulsion; 5:24, cerebral circulation restored; a third convulsion appeared at the same time; 5:40, convulsions had ceased; cat in semicomatose state; 6 p. m., cat able to walk about cage and spent most of time curled up in corner; did not respond to painful stimuli; 11 p. m., cat sleeping with head on paws; snarled when paws were pinched; had difficulty standing on hind legs; next day cat was stupid and lethargic. Moved only a little when painful stimuli were applied.

Crawled to nearest corner of cage if given opportunity. Reflexes were active. No convulsions observed since 5:30. The third day condition was unchanged. Necropsy performed.

Cat 4.—3:15, etherized; 3:30, vertebral arteries tied, at point just below scalene tubercle and brachial plexus, ligatures passed about carotids; 3:51, carotids occluded; stopped breathing; artificial respiration begun; 4, two convulsive respiratory gasps per minute; 4:11, carotids opened; 4:14, slight convulsions of lower limbs; 4:16, extensor rigidity of lower limbs occurring in spasms; 4:20, extensor rigidity almost continuous in fore legs. Reflexes just beginning to return; 4:50, stood up, legs too weak, fell over on side. Fore legs remained extended. Hind legs flexed and weak; 7, cat sleeping peacefully in cage. When poked, woke up, but did not rise or make effort to move from disturbing influences. When stroked with hand, back arched up. When stroking stopped, cat immediately relapsed into stupid state. Pinching toes scarcely bothered it; it did not try to get away. If put on back remained in that position; appeared to initiate no activities. Did not even eat. Next day wound was healing well; no infection, no swelling. Drank water but did not eat. Cat much as before. Made little response to stimuli. Showed no capacity for sustaining any emotional reaction. Third day; same as before and continued to be until sixth day when it was a little less automatic and stupid. Seventh day autopsy was done in routine manner.

Cat 8.—10:45 a. m., etherized; 11, carotid and vertebrals exposed; vessels occluded; 11:30, after thirty seconds, breathing stopped for thirty seconds. Rhythm was normal for about four minutes and then became increasingly rapid, shallow and labored; 11:37, respiration rate 70 per minute. Slow nystagmus. One generalized contraction of whole body at 11:40; 11:53, convulsions clonic and tonic type; 11:53½, cerebral circulation restored; 11:54, quickly recovered normal respiration. Stupid and apathetic. Next day: cat stupid and apathetic. Crawled into corner when left alone. Responded immediately to petting. Became angry easily. Third day condition much the same. No initiative. 3:30, necropsy was done in routine manner.

Cat 14.—11:08, etherized; vessels exposed; 11:53, vessels occluded; artificial respiration by tracheal cannula started; animal stiffened out immediately; respirations disappeared at the end of thirty seconds; 12:02, generalized clonic convulsions; 12:03, cerebral circulation restored; convulsions continued until thirty seconds after restoration of circulation; 12:08, almost normal respiration reappeared; artificial respiration stopped; 12:10, cat developed marked extensor rigidity of all legs; 12:18 extensor rigidity interrupted by a clonic convulsion which lasted until 12:19 when position of extensor rigidity was resumed; cat unconscious—did not respond to painful stimuli; eye reflexes present but deep reflexes not elicited; 12:30, extensor rigidity practically disappeared; cat lay with head on paws and hind legs curled up under it. Responded extremely sluggishly to painful stimuli; 12:35, attempted to walk but failed and fell on side and then curled up again on head and paws; 12:50, cat developed violent convulsions which alternated with spells of excitement in which cat ran up the side of the cage, banged head against roof but kept on running in spite of the fact he was not making any headway. He continued in this behavior until exhausted and then dropped to the floor. In a few minutes it would recover and repeat this performance. This behavior continued until 1:15; at 2 p. m. cat repeated the performance; 2:10, spells had ceased and cat lay with head buried in corner of cage; 6 p. m., cat still lay in corner with head buried in paws. When picked up, it immediately crawled back into corner. Merely meowed a little when painful

stimuli were applied; did not seem to localize them. The second day: cat lay on side with legs extended. They appeared to be slightly rigid. Cat purred when petted but scarcely responded to painful stimuli; would not eat food placed in front of him but would swallow if spoon fed. Necropsy done twenty-eight hours after termination of occlusion period.

CAT 22.—9:55 a. m., etherized; vessels exposed; 10:30, carotid and vertebrals occluded; artificial respiration through tracheal cannula started; respiration ceased at once; pupils dilated; corneal reflexes absent; 10:31, severe convulsions of tonic and clonic type. Convulsions persisted in spite of the fact that cerebral circulation was restored at 10:31. Animal finally died of exhaustion at 11:30. Necropsy done in routine manner. (This is an excellent example of acute death from convulsions.)

CAT 23.—3 p. m., etherized; vessels exposed; 3:35, carotid and vertebrals occluded; 3:36, generalized clonic convulsions lasting ten seconds; occasional convulsive respirations; 3:41, cerebral circulation restored; 3:42, convulsive movements of both hind legs; 3:50, normal respiration reappeared; 3:55, developed series of violent convulsions of clonic type; in state of extensor rigidity between attacks; 4:05, convulsions ceased; cat able to walk about cage; stupid; not able to localize painful stimuli; deep reflexes difficult to elicit; eye reflexes returned. Next day, cat extremely stupid. Spent most of the time lying with head in corner of cage. Would move about if sufficiently stimulated. No initiative; scarcely responded to painful stimuli; did not seem to localize the source of irritation. Necropsy done in routine manner twenty-four hours after termination of occlusion period.

CAT 27.—3:55, etherized; vessels exposed; 4:25, carotids and vertebrals occluded; artificial respiration through tracheal cannula started; 4:26, respiration stopped; 4:29, all reflexes disappeared; 4:30, vessels relaxed; 4:35, respiration returned but only as convulsive gasps; 4:45 respirations almost normal—tracheal cannula removed; 4:55, cat developed slight extensor rigidity of fore legs; 5:30, cat lay with head on paws, did not respond to noises. Painful stimuli, scarcely made it move at all; merely snarled a little. Second day, stupid; did not localize painful stimuli or make serious attempt to escape from irritation. Third day, continued to be stupid, reaction to stimuli although immediate consisted only of snarling. Fourth day, slightly less stupid but still lethargic in reaction to painful stimuli. Reactions were all immediate; that is when pinched it snarled and appeared angry but if petted, did not seem to remember pain and at once began to purr and arch up its back. Sixteenth day, had partially recovered normal behavior but continued to be a little stupid and to forget quickly painful stimuli. Necropsy done in routine manner.

CAT 32.—10:30, etherized; vessels exposed; 11:30, carotids and vertebrals occluded; artificial respiration; 11:31, respiration stopped; 11:33, severe clonic convulsions lasting one minute; 11:34, cerebral circulation restored; repeated clonic movements of both hind legs which continued until 11:35; 11:36, normal respiration returned; tracheal cannula removed; 11:37, severe generalized convulsions—duration half a minute; 11:38, marked extensor rigidity; cat comatose; painful stimuli produced no response; reflexes absent; 11:41, brief convulsion of clonic type; 4 p. m., cat lay with head on paws; when pinched got up and crawled to another corner but made no attempt to localize painful stimuli; second day, cat almost normal. Stupidity not so evident as in other cats that had convulsions much less severe than those experienced by this animal. Third day, condition unchanged. Only slight sluggish reaction to painful stimuli. Necropsy done in routine manner.

EPILEPSY IN ADULTS

RESULTS OF TREATMENT BY KETOGENIC DIET IN ONE HUNDRED CASES *

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The fact that hypotheses and methods of treatment for epilepsy are constantly changing, each as it is advanced being tried and found wanting, causes a healthy disbelief in any new form of treatment. Time alone will supply substantial reasons for altering what may be termed the traditional treatment for epilepsy.

The use of diets high in fat and extremely low in carbohydrate in the treatment for idiopathic epilepsy was first suggested by Wilder [1] as a possible substitute for the fasting regimen which had previously been shown by Guelpa and Marie [2] and by Geyelin [3] to influence seizures in many cases. Wilder originally proposed the diet on the theory that aceto-acetic acid should behave pharmacologically as an anesthetic. In such an event, the diet might act only as a palliative measure similar to the action of phenobarbital, and the value of a regimen that necessitated so much effort and sacrifice on the part of patient and physician would hardly be a worthy substitute for sedative drugs.

Other observers believe that a diet high in fat owes its therapeutic value to its effect on the acid-base equilibrium by correcting an abnormal tendency toward the spontaneous development of alkalosis. It probably has an even more fundamental influence on the balance of the basic elements of the nervous tissues, namely, water and fat, and may thus alter the conductivity of the nerve cell. Lennox and Cobb,[4] in their comprehensive monograph, presented the many physiologic factors, such phenomena as anoxemia, alkalosis or edema, that may precipitate

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* From the Division of Medicine, the Mayo Clinic.

1. Wilder, R. M.: The Effects of Ketonemia on the Course of Epilepsy, Mayo Clinic Bull. 307, 1920-1921, vol. 2.

2. Guelpa, G., and Marie, A.: La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire, Rev. de thérap. méd.-chir. **78**:8, 1911.

3. Geyelin, H. R.: Fasting as a Method of Treating Epilepsy, M. Rec. **99**: 1037, 1921.

4. Lennox, W. G., and Cobb, Stanley: Medicine Monographs: Epilepsy, Baltimore, Williams & Wilkins Company, 1928, vol. 14, pp. 35-42, 59-76, 89-143, and 147-151.

seizures by a general, widespread change in brain tissue. Fay,[5] and later McQuarrie,[6] called attention to the possible influence of fluid and its control in the treatment for epilepsy.

All three steps—fasting, the ketogenic diet and rigid restriction of intake of fluid—have in common the effect of dehydrating the tissues and a tendency to maintain the hydrogen-ion concentration of the body fluids at a slightly higher level than normally exists. Dehydration alone produces a shift in the acid-base balance toward the acid side. This intimate relationship of the acid-base balance and the water balance makes it difficult to ascertain which is of primary importance, so far as the occurrence of seizures is concerned.

During the last eight years, in the Mayo Clinic, the ketogenic diet has been used in the treatment of adults suffering from idiopathic epilepsy. Since 1924, an effort has been made to select cases on the following criteria: (1) The case must be one of idiopathic epilepsy (that is, the type of epilepsy in which known organic causes of the recurrent convulsions have been eliminated); (2) the patient must have the intelligence and willingness to cooperate to the fullest extent; (3) the patient must be in a suitable environment and have facilities to secure the diet; (4) the attacks of either petit mal or grand mal must be frequent enough to justify certain statistical conclusions, over a period of years, regarding the benefit that may or may not be derived, and (5) the patient must be willing to spend two or three weeks under the physician's direct supervision so that he may learn individually the manner of maintaining and adjusting the ketogenic diet. If any degree of benefit is to be hoped for, the education of the patient is as important a measure in the treatment for epilepsy as in the treatment for diabetes mellitus.

This report is made on the first one hundred cases of epilepsy since 1924 in adults who were placed on the ketogenic diet alone, the purpose being to ascertain if there was any merit from the diet in such cases. The report is considered in two parts: first, that relating to the varied experiences from the use of the ketogenic diet and, second, that concerning the results from the use of the ketogenic diet in one hundred cases.

EXPERIENCE WITH THE KETOGENIC DIET

Since treatment for epilepsy by diet must perhaps be continued throughout a long period, it is extremely important to guard against the possible evil effects of any kind of deficiency in diet. Adequate

5. Fay, Temple: Some Factors in the "Mechanical Theory of Epilepsy" with Especial Reference to the Influence of Fluid, and Its Control in Treatment of Certain Cases, Am. J. Psychiat. **8**:783, 1929.

6. McQuarrie, Irvine: Epilepsy in Children, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

calories, protein, minerals and vitamins must be provided for maintenance of the adult and for growth of the child. Although studies have not revealed definite evidence of harmful effects from the diet, certain observations have been made that are worthy of attention.

There is a negative balance of calcium and phosphorus in the ketogenic diet. In the Mayo Clinic, therefore, small doses of calcium lactate are incorporated.

Because of the fact that ketosis taxes the protein molecule for its antiketogenic fraction, it is perhaps best to use from 1 to 1.5 Gm. of protein for each kilogram of body weight in order to maintain nitrogen equilibrium, the amount depending on the age of the patient and the degree of ketosis produced. A few young adults have derived distinct benefit by having their seizures controlled over a period of from one to three years, and they have gradually become refractory to the ketogenic diet. It is possible that these patients became so because of partial protein starvation in the presence of severe ketosis, and thus a tendency toward abnormal hydration of the tissues has developed, a factor diametrically opposed to one of the objects of the diet.

Because of possible lack of vitamin B in the diet, I have incorporated as a routine from half to one teaspoonful of brewers' yeast daily.

Of fifty-six women treated by the ketogenic diet, twelve had cessation of the menses. This observation calls attention to the possible effect on the hormones of a diet high in fat, or perhaps a deficiency of vitamins B and E, that may influence the menstrual cycle. It also brings up the question as to whether the menses will return after resumption of a more normal diet. Seven patients whose menses had ceased were allowed to resume a normal diet, and within a few months there was a return of normal menstrual periods. In one case of epilepsy with associated menorrhagia and without any pathologic condition demonstrable in the pelvis, there was complete cessation of the flow for one year. When the patient was put on a normal diet the menses returned, but without menorrhagia up to the present time, a period of eleven months.

Campbell [7] and others stated that blood cholesterol is above normal in starvation, in diets high in fat and during pregnancy, three factors that tend to diminish seizures. Okey and Boyden [8] called attention to the lowered cholesterol at the premenstrual period, a time when seizures tend to be more frequent. A number of investigators [9] have found that the level of cholesterol, both in blood and in plasma, is low or

7. Campbell, J. M. H.: Cholesterol in Health and Disease, Quart. J. Med. **18**:393, 1925.

8. Okey, Ruth; and Boyden, Ruth E.: Studies of the Metabolism of Women: III. Variations in the Lipoid Content of Blood in Relation to the Menstrual Cycle, J. Biol. Chem. **72**:261, 1927.

9. Robinson, S. H. G.; Brain, W. R., and Kay, H. D.: Association of Low Blood Cholesterol with Occurrence of Fits in Epileptics, Lancet **2**:325, 1927.

falling prior to the seizures; also that the average level is lower in epileptic than in normal persons. I confirmed these observations of low cholesterol values in epileptic persons; after they have been on the ketogenic diet, a gradual rise to and above normal occurs. Certain authors believe that protoplasm has the property of phase reversal. Two vitally significant constituents of protoplasm are cholesterol and lecithin, which play an important part in the membranes of the cell. The fact that the nervous tissue is made up of only water and fat, and that changes have been found in the proportion of cholesterol and lecithin in the blood stream, brings up for consideration experimental work in the field of colloidal chemistry, considering the nervous tissue as a two-phase system of water solution and lipin solution, with changes in the excitability of the nerves and in the permeability of the cell, dependent on which phase is predominant.

In a few cases the institution of the ketogenic diet increased markedly the frequency and severity of seizures.

Guelpa noted a change in the mental demeanor of patients who fasted. Pediatricians have called attention to this,[10] and I have noted clinically that the mental conception was clearer, that there seemed to be a more alert and intelligent expression and a more normal attitude and that many patients were definitely less irritable.

Another observation is the comparative freedom from the common acute infections and colds. This may be due to the high content of butter in the diet.

Two cases are worthy of note in that overindulgence of fluids precipitated convulsive seizures.

In three cases there was a reversion of the epileptiform seizures into severe attacks of migraine.

Diets high in fat have been reported by Smith[11] to be somewhat laxative. Constipation is almost a constant symptom in epilepsy. Fifty-six patients in my series were benefited by the ketogenic diet; forty-one of these patients did not have further trouble with constipation. In the forty-four cases in which the epilepsy remained unchanged, benefit was derived in thirteen, so far as constipation was concerned.

Of the one hundred patients, sixty-six did not complain of hunger after the first few days; thirty-four had difficulty because of hunger.

Forty-seven of the fifty-six women were able to do their usual work while on the diet. Only twenty-seven of the forty-four men were able to do their usual work while on the diet. This was probably due to the greater physical demands made on the men.

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10. Helmholz, H. F.: The Treatment of Epilepsy in Childhood, J. A. M. A. **88**:2028 (June 25) 1927.

11. Smith, Florence W.: The Use of High Fat Diets in the Treatment of Constipation, Proc. Staff Meetings Mayo Clinic **2**:166, 1927.

DATA CONCERNING CASES

The patients in this series have been on the ketogenic diet from three months to five years. For purposes of study, the cases have been tabulated in three groups: (1) cases in which the attacks have been controlled by the ketogenic diet; (2) cases in which there has been definite improvement by lessening the frequency or severity of attacks, and (3) cases of failure. The ages varied from 16 to 51 years, and the attacks varied in duration from one year to thirty-two years prior to the time of treatment.

TABLE 1.—*Observations on Patients Whose Condition Had Been Controlled*

Case	Age and Sex	Diagnosis	Attacks Before Treatment	Disease, Years	Diet, Mo.	Comment
1	19 F	Grand mal Petit mal	About every six weeks Irregular intervals	9	20	One attack since on diet, December, 1928
2	18 F	Grand mal Petit mal	Twice a day every ten days	15	12	No attacks since on diet; now on normal diet
3	18 F	Grand mal Petit mal	Four to eight a year Irregular intervals, two to six weeks	14	20	No attacks since on diet
4	51 M	Grand mal	Every two to four weeks	12	12	No attacks since on diet
5	21 M	Grand mal Petit mal	Every ten days Irregular intervals	5	20	No attacks since on diet
6	19 M	Grand mal	Every two to four months	5/6	12	No attacks since on diet
7	42 M	Grand mal Petit mal	One or two yearly Rather frequently	10	27	No attacks since on diet; patient died of pneumonia, 1928
8	34 F	Petit mal	Once a month; about eight spells in a day	7	24	No attacks since on diet; has not been on diet for seven months
9	42 M	Grand mal Petit mal	One to two, for three to four days each month Three to seven, for three days each month	32	46	Little improvement for first eight months; one attack since Aug. 15, 1926
10	39 F	Grand mal	Every two to four weeks	5	24	Attacks lessened to one every seven to nine weeks for first eight months; no attacks for last twenty-eight months; has not been on strict diet for the last twelve months
11	32 F	Petit mal	Two to three attacks every twenty-four hours	2	39	Three attacks in first three months while on diet; none since; has not been on strict diet for six months
12	16 F	Grand mal	Several in daily succession every three weeks	5	16	No attacks since on diet

Twelve of the one hundred patients have controlled their attacks by the use of the ketogenic diet (table 1). Eight of the patients have not had attacks since ketosis developed. These patients have remained in constant ketosis for from twelve to twenty-seven months. Two of the eight patients have been allowed gradually to return to a qualitative, unweighed diet, merely emphazing the restriction of gross starches and sugars. As yet, attacks have not returned although they have been rather expected.

One patient (case 9) derived little benefit for several months; then attacks gradually lessened, and only one attack has occurred since 1926.

TABLE 2.—*Observations on Patients Benefited*

Case	Age and Sex	Diagnosis	Attacks Before Treatment	Disease, Yr.	Diet, Mo.	Ketosis	Comment
13	24 M	Grand mal Petit mal	Once a month Series of three to seven every two to four weeks	2.5	42	Always present	Diet controlled attacks for two years; then attacks returned in mild form every three to six months
14	37 F	Grand mal	Once a month	9	36	Always present	Four attacks since on diet
15	35 F	Petit mal	Several attacks daily	24	32	Always present	Gradual improvement after being on diet for three months; attacks now occurring in series every two months
16	31 M	Grand mal Petit mal	Once a month Daily, sometimes six to seven a day	2	30	Always present	No attacks of grand mal; attacks of petit mal once a month
17	20 F	Grand mal Petit mal	Grand or petit mal often every day; might be an interval of from one to two weeks	6	40	Always present	Attacks completely controlled for three years; now, attacks return every three to six weeks
18	19 F	Grand mal Petit mal	Every three to six weeks Every two to three weeks	10	19	Always present	One attack of grand mal and six of petit mal since on diet
19	18 F	Grand mal Petit mal	One every two weeks, more often at intervals Daily	4.5	36	Always present	No attacks for two and a half years then became refractory to diet
20	56 M	Grand mal Petit mal	One or two a month Frequent	20	17	Never present	Has had but three attacks since on diet
21	18 M	Grand mal Petit mal	Grand or petit mal every day	3	11	Always present	One attack since on diet
22	15 M	Grand mal Petit mal	From one attack in two weeks to twenty in a day	1	12	Periodic	Has had three attacks since on diet
23	19 F	Petit mal	Seven to ten daily	9	7	Never present	Only one or two attacks of petit mal daily
24	17 F	Grand mal	One attack every three weeks	0.5	7	Periodic	Three attacks since on diet
25	22 F	Grand mal Petit mal	One a week to one a month Daily	8	22	Always present	No attacks of grand mal since on diet; petit mal much improved but not controlled
26	19 F	Grand mal	Two to three a month	4	9	Never present	One attack a month, less severe in type
27	15 F	Grand mal	One every three to four weeks	6	12	Always present	Attacks once every three months
28	24 M	Petit mal	Several daily	13	10	Always present	Attacks less frequent; now controlled for three months
29	17 F	Grand mal Petit mal	Three or four a year Daily	13	19	Periodic	No attacks of grand mal since on diet; petit mal less frequent and less severe
30	24 F	Grand mal Petit mal	One attack a week Daily	6	6	Never present	Attacks less frequent; usually at time of menstruation
31	26 F	Grand mal Petit mal	Four or five a year Daily	2	8	Always present	One grand mal since on diet; petit mal much less frequent
32	24 F	Grand mal	Every two to four weeks	12	7	Periodic	Attacks about every two and a half months; less severe
33	17 M	Grand mal Petit mal	One to eight each month Daily	5	19	Always present	Has had only three or four attacks which were rather light and incomplete since on diet
34	42 M	Grand mal Petit mal	From four to six a month Daily, too numerous to count	20	20	Always present	Four attacks of grand mal since on diet; petit mal about every thirty days
35	15 M	Grand mal	One a month	3	6	Always present	One attack since on diet

TABLE 2.—*Observations on Patients Benefited—Continued*

Case	Age and Sex	Diagnosis	Attacks Before Treatment	Disease, Yr.	Diet, Mo.	Ketosis	Comment
36	15 M	Grand mal	One every six weeks	2	8	Always present	Three attacks since on diet; attacks much lighter
37	27 F	Grand mal	One each month	11	6	Periodic	One attack since on diet; now on qualitative regimen; no attacks for one year
38	33 M	Grand mal	Every two to four weeks	10	6	Never present	No attacks while on strict diet; now on qualitative diet for one year; attacks every ten weeks
39	20 F	Grand mal Petit mal	About two a month Irregular intervals	5	15	Always present	One attack since on diet
40	19 M	Grand mal	One a month	2	14	Periodic	Three attacks since on diet
41	20 M	Grand mal	One or two each month	5	9	Periodic	Two attacks since on diet
42	25 M	Grand mal	One a month	3	6	Periodic	Two attacks since on diet; these very light
43	16 M	Grand mal	From one to four a week	3	6	Never present	Diet only qualitative; attacks less severe and only about one a week
44	31 F	Grand mal Petit mal	About every ten days	18	6	Never present	Diet only qualitative; attacks much less severe, mostly petit mal, in series, once a month
45	21 F	Grand mal Petit mal	Began in 1924; one attack monthly Many times for eight years	8	24	Always present	Two attacks since being on diet
46	19 F	Grand mal Petit mal	Only two attacks, 1923-1925 Light attacks every few minutes	6	30	Always present	No attacks of grand mal; petit mal has almost disappeared; now on qualitative diet
47	26 F	Grand mal	One attack each month	1	40	Periodic	No attacks while on diet; has broken diet five times, each time followed by attack
48	34 F	Grand mal Petit mal	Grand or petit mal several times a week	18	31	Always present	Not controlled but attacks reduced to about one every two weeks
49	22 F	Grand mal	Three or four a year	5	30	Periodic	Two attacks one and a half years apart
50	33 M	Grand mal	Every twenty-five to forty days regularly	4	30	Periodic	Breaks diet periodically; attacks every three to four months
51	20 F	Grand mal Petit mal	Every night From three to seven daily	5	32	Periodic	Since on diet has one or two attacks a week with periods of freedom for a month
52	25 F	Grand mal Petit mal	Average one a month One a week	11	30	Periodic	Average two or three attacks a year
53	18 F	Grand mal Petit mal	Had six attacks Many daily	2	8	Periodic	One attack of grand mal; attacks of petit mal every two or three weeks
54	38 M	Grand mal Petit mal	Every two months Daily	2	15	Always present	Attacks once every four months until July, 1929; no attacks since
55	30 F	Grand mal	Two or three attacks a month	18	15	Always present	About one attack every two months
56	18 F	Grand mal Petit mal	Two attacks a week Daily	3	8	Periodic	One attack first month on diet; no attacks since

Two patients (cases 10 and 11) were slow to derive benefit but after being free from attacks for more than two years, with a previous history of rather frequent attacks, they were gradually allowed to return to a diet with qualitative restriction only.

Forty-four patients (table 2) have been definitely benefited; seizures are less frequent and less severe. Four patients (cases 13, 15, 17 and 19) are deserving of special mention, as the condition was con-

TABLE 3.—*Observations in Failures*

Case	Age and Sex	Diagnosis	Attacks Before Treatment	Disease, Yr.	Diet, Mo.	Ketosis	Comment
57	27 F	Grand mal Petit mal	Once or twice a month Weekly	6	3	Periodic	Diet three months; no change noted, now uses phenobarbital also and has had two major attacks since July, 1927
58	20 M	Grand mal	Every two or three weeks	17	7	Most of the time	No improvement in control of attacks but definite change in mental demeanor
59	21 M	Petit mal	Attacks vary from daily series to one or two in six months	7	7	Periodic	Failed to be of any benefit
60	19 F	Petit mal	From one to five a week	16	3	Present	Attacks more frequent; no benefit
61	32 M	Grand mal Petit mal	One a month Every three to four days	22	22	?	No change
62	27 F	Grand mal Petit mal	Every two to four months Once or twice daily	13	6	Periodic	About the same
63	34 F	Petit mal	From one to four daily	6	4	Periodic	No benefit
64	19 F	Petit mal	Vary from three daily to three to eight a month	5	13	Present	No apparent benefit
65	22 F	Grand mal Petit mal	Grand mal or petit mal once a month	3	8	Periodic	No attacks of grand mal, but still has petit mal; used phenobarbital occasionally
66	37 F	Petit mal	Once a week	24	6	Present	No change in number of attacks
67	45 M	Grand mal Petit mal	Once a month Once a week	15	3	?	Attacks about as regular though less severe
68	30 M	Grand mal Petit mal	From one to three a month As often as two a day	29	6	?	No apparent change
69	19 M	Grand mal Petit mal	Grand and petit mal vary; three or four attacks a week	16	6	Seldom present	About the same; had very severe attack at end of six months and stopped diet
70	23 M	Grand mal	One a week	15	3	Always present	Attacks less often but more severe
71	26 M	Grand mal	Twice yearly	16	7	Always present	Diet caused increase in attacks to one or two a month
72	15 F	Grand mal	From one to seven months apart; precipitated by drinking large amounts of water	9	1	Never present	Failed to cooperate
73	19 F	Grand mal Petit mal	Every five weeks Irregular periods	3	12	Always present	Grand mal every six weeks to two months; from one to four or five attacks of petit mal a day

trolled for from two to three years and then they became refractory to the diet while remaining in strict ketosis.

Forty-four patients (table 3) did not derive benefit from the procedure. Nine patients had attacks more frequently. Four of these

TABLE 3.—*Observations in Failures—Continued*

Case	Age and Sex	Diagnosis	Attacks Before Treatment	Disease, Yr.	Diet, Mo.	Ketosis	Comment
74	16 M	Grand mal	Two a week	5	12	Never present	No change in condition
75	15 F	Grand mal	Two a year	1	9	Never present	No attack for six months, then attacks became more frequent
76	16 F	Grand mal Petit mal	Both varied greatly from six a day to one a month	5	9	Never present	Attacks somewhat improved at first; after six months became much worse
77	33 M	Grand mal	One every three months	15	18	Always present	Four attacks first year; no attacks during last six months
78	17 M	Grand mal Petit mal	In series, every six to seven weeks	7	3	Always present	No benefit
79	17 F	Petit mal	Daily	3	2	Never present	Attacks more frequent while on diet
80	27 M	Grand mal	From one to six months	3	8	Never present	Very little improvement
81	23 M	Grand mal	From one to five a month	2	6	Periodic	Attacks less frequent while on diet but patient unable to work
82	21 F	Grand mal	Five a year	5	2	Never present	One attack about every six weeks
83	24 F	Grand mal	One every six weeks	8	4	Never present	No marked benefit evidenced
84	26 F	Grand mal	Several attacks at menstrual period	12	14	Always present	No attacks during first three months; then returned at time of menstruation; patient thinks attacks less severe
85	32 M	Grand mal	From ten to twelve a month	15	3	Never present	Attacks became much more frequent
86	46 M	Petit mal	From two to five daily	4	12	Never present	Very slight improvement
87	23 F	Grand mal	Daily	7	10	Periodic	Attacks just as frequent but less severe
88	17 F	Grand mal	More or less every month	4	5	Always present	Attacks more frequent while on diet
89	17 F	Grand mal Petit mal	Every three months Daily	10	6	Never present	No benefit
90	49 M	Grand mal	Twice a year	7	4	Never present	One light attack since on diet
91	36 M	Grand mal	From six to eight a year	3	3	Never present	Too short a time to judge; would consider a failure
92	19 F	Petit mal	Eight a month	14	3	Never present	Attacks increased after diet
93	22 F	Grand mal Petit mal	Grand and petit mal twice a week	8	26	Periodic	Six attacks since on diet; these occurred when patient was off accurate diet
94	22 F	Grand mal Petit mal	From four to nine a month	5	6	Never present	From four to seven attacks a month; no benefit
95	19 M	Grand mal Petit mal	One to two a day	13	6	Never present	No benefit from diet
96	17 F	Grand mal	Every two weeks	13	5	Never present	Attacks every two weeks; no benefit
97	23 M	Grand mal Petit mal	From one to four a month From two to three daily	10	12	Never present	No benefit
98	17 F	Grand mal	From seven to eight a month	11	12	Always present	Attacks were lighter but just as frequent
99	19 M	Grand mal	About ten a month	7	6	Always present	Attacks increased in frequency but became less severe
100	22 M	Grand mal Petit mal	From three to four a month Daily	10	8	Never present	No benefit

patients (cases 60, 71, 88 and 99) maintained constant ketosis from three to seven months, while the remaining five were practically never in ketosis. Five patients maintained the diet accurately and were in a state of ketosis for from three to eighteen months without any change in the attacks.

COMMENT

It is important to note (table 4) that of the twelve cases that were controlled, diacetic acid, tested for daily, was always present in eleven cases and was present intermittently in one case. In forty-four cases in which the condition was improved, ketosis was maintained in twenty-two; in fourteen it was periodic, and in eight diacetic acid was never present, but these patients were on a qualitative diet high in fat and low in carbohydrate. Of the forty-four patients not benefited, thirteen maintained the diet accurately and were in a state of ketosis for from three months to eighteen months without any change in the attacks. In eight cases the patient admitted that ketosis was periodically or

TABLE 4.—*Ketosis*

	Cases	Always Present	Periodic	Always Absent
Controlled	12	11	1	..
Improved	44	22	14	8
No benefit	44	13	8	23

questionably present, and in twenty-three cases ketosis did not develop. It seems fair to assume that some of the failures might be due to improper management of the diet or lack of ketosis, but probably it is more fair to assume that the results are failures unless proved otherwise.

There seems to be no question but that the patient who can be afforded the best opportunity for treatment is the child or young adult who is just beginning to have seizures, before the convulsive reaction has become a habit; whereas older patients, or those who have had attacks frequently for years, especially with resultant mental deterioration, are the least likely to be benefited.

If the results in these one hundred cases have been interpreted properly, the benefit derived, although not encouraging or conclusive, seems fairly worth while; namely, in twelve cases the condition was controlled and in forty-four cases the patient was distinctly benefited. This percentage of benefit seems sufficiently encouraging to warrant further trial or study of the ketogenic diet experimentally. I realize that the ketogenic diet cannot be used as a routine because of certain

difficulties previously reported.[12] It is not possible because of economic, financial and mental reasons, to place all patients on a strict diet. An interpretation of results cannot be made that is not subject to error. There are factors in epilepsy, such as the incidental cessation of seizures, which must be taken into consideration. It should be recommended, therefore, that if the ketogenic diet is used therapeutically it be used in conjunction with the restriction of fluids, and with other measures at our disposal.

TABLE 5.—*Summary of Cases*

Controlled by ketogenic diet	12
Definitely improved by diet	44
Total deriving benefit	56
Cases deriving no benefit	44
Total cases on ketogenic diet	100

SUMMARY

One hundred adult patients, not observed in institutions, who were suffering from idiopathic epilepsy, were treated with a ketogenic diet. In twelve cases the attacks were controlled, and in forty-four the patients were definitely improved; thus, fifty-six patients were benefited by the diet. Forty-four patients were not benefited and the treatment was considered a failure, although a number of patients were not maintained in a state of ketosis. The results are summarized in table 5.

12. Barborka, C. J.: Ketogenic Diet Treatment of Epilepsy in Adults, J. A. M. A. **91**:73 (July 14) 1928; The Ketogenic Diet and Its Use, M. Clin. North America **12**:1639, 1929.

EPILEPSY

EVIDENCES OF BODY FLUID VOLUME DISTURBANCE*

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During the course of studies of the acid-base metabolism of epileptic children carried out some years ago with Ross and Tisdall [1] and with Hamilton,[2] data were obtained which suggest a disturbance of the volume of body fluid in this disease. The pretext used for briefly recalling these bits of evidence is the recent interest in the effect of the restriction of water in epilepsy which has been aroused by the work of Fay and of McQuarrie.

OBSERVATIONS

The data that will first be considered were obtained from fasting epileptic children.[1] An item of the study of these children was an attempt to measure the factors of loss of body weight during fasting. The weight of body protein consumed, of course, can be estimated from the amount of nitrogen entering the urine. An estimation of the weight of fat burned can be derived from measurements of the ketone acid and of the nitrogen excretion. It occurred to me that it should be possible to calculate the remaining factor of the loss of body weight, namely, the loss of body water, from the amount of fixed base found in the urine. The premise used here is that, since the concentration of fixed base in the body fluids tends to remain closely stationary, a loss of fixed base will be accompanied by a parallel withdrawal of body water. In the accompanying table are given the calculated values for these three factors of the loss of body weight during a fifteen day fast derived from measurements of nitrogen, ketone acids and fixed base excreted in the urine. The patient was a girl, aged 8. The loss of body weight directly measured on the scales is also given in the table and agrees closely with the sum of the calculated values.

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* From the Department of Pediatrics, the Harvard Medical School.

* Read before the Association for Research in Nervous and Mental Diseases, New York, Dec. 27, 1929.

1. Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923.

2. Gamble, J. L., and Hamilton, B.: The Acid-Base Composition of Urine from an Epileptic Child, Bull. Johns Hopkins Hosp. **41**:389, 1927.

This outcome encouraged an attempt to obtain more detailed information regarding the loss of body fluid, the results of which are described by chart 1.

The data are for consecutive three day periods of the fifteen day fast of a girl, aged 8. The estimations of the losses of intracellular water which the diagram presents were calculated from the amounts of potassium found in the urine, using here the fact that potassium is contained almost exclusively in intracellular water and taking as the initial datum of the calculation the concentration of potassium in muscle water. The obvious *a priori* explanation of a loss of intracellular body water during fasting is that this event is simply a consequence of consumption of body protoplasm. By calculating the extent of destruction of protoplasm in this subject from measurements of the nitrogen excretion and using the standard value for the water content of muscle protoplasm, estimations of the loss of intracellular body water from this cause were obtained. The values thus found for the

Calculated Values for Factors of Body Weight Loss During Fasting

Calculated Values For:	Gm.
Protein, oxidized	452
Fat, oxidized	1,124
Water lost	2,410
	3,986
Body weight loss directly measured	3,920

first two periods of the fast are considerably less than the losses calculated from the excretion of potassium. The remainder of the loss of intracellular water is thus indicated as deriving from undestroyed protoplasm and may be taken as evidence of a reduction of cell volume. From measurements of the excretion of sodium, and using the widely differing values for the concentration of sodium in extracellular and in intracellular water, the remaining factor of the loss of body fluid, composed of interstitial water, was derived. These calculations obviously contain a considerable amount of assumption, but they are supported by the fact that when all of the values for the several periods are added together, the calculated value for total body loss thus obtained is in satisfactory agreement with the loss directly measured on the scales.

The gist of the evidence which these data provide is that fasting produces a change in the volume of body fluid in the direction of reduction. There is thus presented the possibility that this change in volume may be the event which is beneficial in epilepsy, rather than the change in body fluid reaction (acidosis) which fasting also produces, and which is usually credited as the explanation of the therapeutic effect of fasting. It should be noted here, however, that the

change in reaction is possibly an antecedent factor in the alteration of volume.

The surmise that the changes in volume produced by fasting may bear relationship to the disappearance of the manifestations of epilepsy would be considerably supported by demonstration of disturbance of body fluid volume control in active epilepsy. The succeeding data are suggestive in this direction. They are from a study of the acid-base

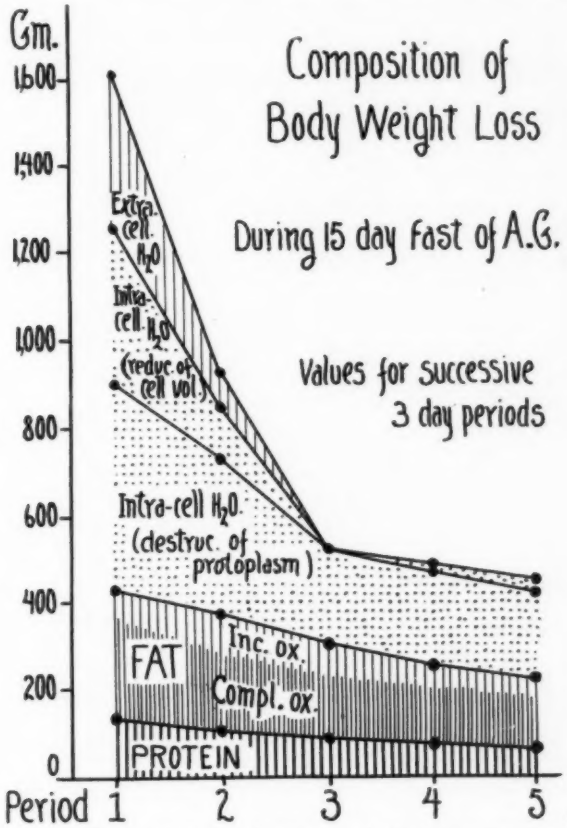

Chart 1.—Composition of loss of body weight for consecutive three day periods of a fifteen day fast, calculated from measurements of nitrogen, ketone acids and potassium in the urine. The individual factors of the weight loss are superimposed in the diagram.

excretion of an epileptic girl, aged 11, and were obtained from consecutive twenty-four hour collections of urine, the diet being constant as regards both composition and daily intake.[2] A stationary level of fluid intake was also maintained. The subject was unusually suitable for this plan of study. There were recurring periods of severe seizures, lasting each time about two days, with intervals between of

from four to seven days. The measurements of excretion of fixed base are presented in chart 2. On the constant intake of fixed base which the diet provided, a nearly stationary value for the daily amount entering the urine would be expected. There occurred, however, as may be seen in chart 2, an irregular excretion with a huge peak on the first day of the periods of seizures. These observations were repeated over several other periods of attacks, and the data obtained were the same as shown here. These data, it is believed, can be

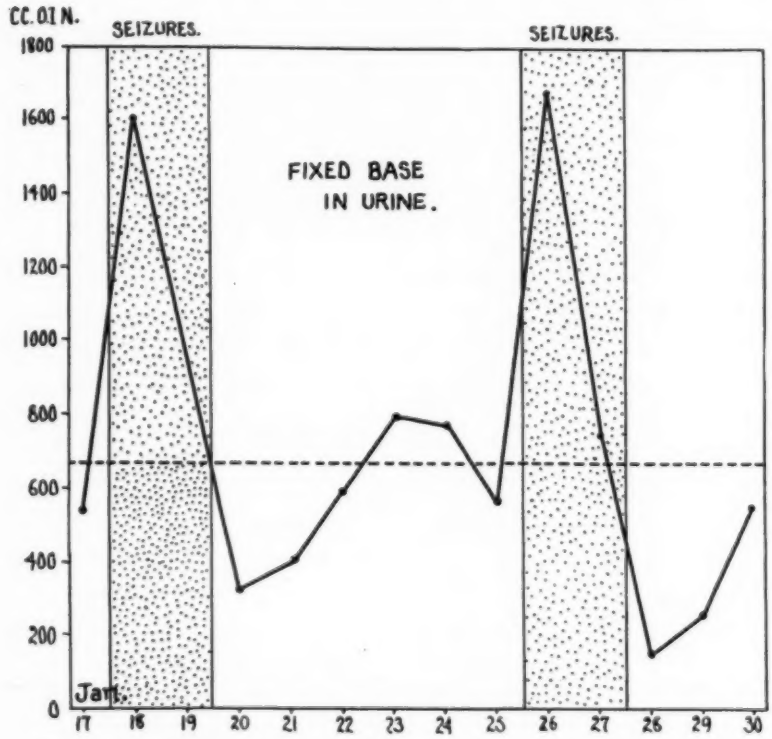

Chart 2.—Measurements of fixed base in consecutive twenty-four hour collections of urine from an epileptic child.

dependably interpreted as describing alternating release and retention of body fluid, release occurring during the periods of seizures. In support of this interpretation there was a rough but definitely corresponding fluctuation in the daily volume of urine. In chart 3 are given measurements, covering a single period of seizures, of the four individual bases—sodium, potassium, calcium and magnesium—which together compose the total fixed base value.[3] It will be seen at once

3. (Gamble and Hamilton: Bull. Johns Hopkins Hosp. **41**:389, 1927.) The values for magnesium indicated in the diagram were obtained subsequently to the publication of the paper here cited.

that the values found for sodium explain the large rise and fall of the excretion of fixed base shown in chart 2; the two small factors, calcium and magnesium, remained nearly stationary, and the values for potassium were at least roughly regular. Since sodium makes up nearly all of the total fixed base contained in extracellular (interstitial) body fluids and is contained to a relatively slight extent in intracellular water, these measurements demonstrate that the body water thrown out during the periods of seizures is of interstitial origin. It may here be noted that in this study no evidence of a loss of intracellular water

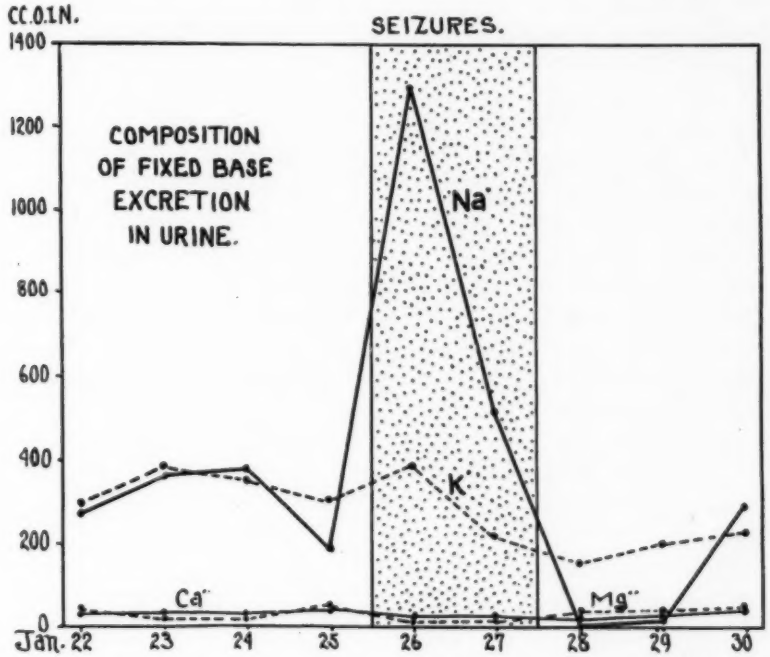

Chart 3.—Analysis of the excretion of fixed base, demonstrating that extension during the period of seizures is composed of sodium.

appeared. These data, therefore, do not indicate that the intracellular traction of the loss of body fluid during fasting is of therapeutic significance.

COMMENT

The results of this study apparently indicate an underlying disturbance of body fluid volume control in epilepsy. An obstacle to this inference, however, must be admitted; namely, that these observations may be simply products of the convulsive state and are therefore without pathogenic significance. Although such an explanation may be regarded as improbable, direct evidence to the contrary is not contained in the data here presented.

THE THERAPEUTIC EFFECT OF DEHYDRATION ON EPILEPTIC PATIENTS*

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The significance of the increased amounts of cerebrospinal fluid found over the frontoparietal areas of the brain in epileptic patients was analyzed and discussed in a former paper.[1] It has seemed possible to correlate many of the isolated physiologic and clinical observations regarding epileptic patients in terms of a common factor, such as fluid, when otherwise no apparent direct relationship existed.

Thus, the observations of Hippocrates[2] that the brains of persons with epilepsy were "unusually moist" may be considered substantiated by those of Alexander,[3] who used direct drainage of the cortex with some degree of success in epileptic patients showing increased collections of subarachnoid fluid. Dandy[4] has repeatedly called attention to these abnormal collections of fluid distributed over the frontoparietal areas of the brain, characteristically found in the patient with chronic epilepsy. Mixter[5] has remarked on the presence of this fluid in excessive amounts in epileptic patients when the brain is exposed at an operation.

The discovery of "cerebral edema" and "wet brain," by the surgeon and the pathologist, associated with acute convulsive manifestations such as eclampsia, uremia, trauma and acute alcoholism, has long been recognized.

The frequency with which these increased collections of supracortical fluid have been demonstrated in the epileptic patient by encephalog-

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* From the Department of Neurosurgery, Temple University School of Medicine, and the Daniel J. McCarthy Foundation.

1. Fay, Temple: Problems of Cerebrospinal Pressure, S. Clin. N. Amer. **4**: 227 (Feb.) 1924.

2. Hippocrates: On the Sacred Disease, translated by Francis Adams, New York, William Wood & Company, 1886, vol. 2, p. 334.

3. Alexander, William: The Surgical Treatment of Some Forms of Epilepsy, Lancet, **2**:932 (Sept. 30) 1911.

4. Dandy, W. E.: The Space Compensating Function of the Cerebrospinal Fluid: Its Connection with Cerebral Lesions in Epilepsy, Bull. Johns Hopkins Hosp. **34**:245 (Aug.) 1923.

5. Mixter, W. J.: Three Cases of Focal Epilepsy, Tr. Boston Neurological Society, Arch. Neurol. & Psychiat. **9**:402 (March) 1923.

raphy has recently attracted much attention. Dandy,[6] Wartenberg,[7] Carpenter [8] and many others have pointed out this fact, and the observations have been accepted as extremely common in the epileptic patient. By means of an improved roentgenographic method devised by Pendergrass [9] and the standardization of the procedure of encephalography presented and discussed in detail by Pancoast and me,[10] it is now possible to visualize clearly the subarachnoid spinal fluid spaces and to compare the roentgenographic films in one case with those in another.

In our studies the epileptic patient has shown abnormalities of the subarachnoid fluid spaces over the frontoparietal regions of the brain, even in the early manifestations of the symptom-complex (fig. 1). An increase in supracortical fluid above the normal volume has been a constant observation in the well established case (Fay,[11] Pancoast and Fay [10]). The operative verification of these observations correlated with the neuropathologic observations of Winkelman [12] has led to the consideration of these collections of subarachnoid fluid in the light of deficiencies in the fluid-eliminating mechanisms, chiefly the subarachnoid villi and pacchionian bodies.

Many recent physiologic observations have indicated that excessive intake of fluid predisposes the experimental animal to convulsive seizures. Rowntree's [13] reports on "water intoxication" indicated that when large quantities of fluid were given to a dog by a stomach tube, typical convulsive seizures were produced and the animal might die in status within from four to five hours.

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6. Dandy, W. E.: Impressions of the Pathology of Epilepsy from Operations, Am. J. Psychiat. **6**:519 (Jan.) 1927.

7. Wartenberg, R.: Encephalographische Erfahrungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:585, 1924-1925.

8. Carpenter, E. R.: Encephalography: Lumbar Puncture and Trephine Methods, Am. J. M. Sc. **173**:333 (March) 1927.

9. Pendergrass, E. P.: New Arrangement of the Bucky Diaphragm for Encephalography, Am. J. Roentgenol. **29**:482, 1928.

10. Pancoast, H. K., and Fay, T.: Encephalography: Roentgenological and Clinical Considerations for Its True Use, Am. J. Roentgenol. **21**:421 (May) 1929.

11. Fay, T.: Some Factors in the "Mechanical Theory of Epilepsy," with Especial Reference to the Influence of Fluid, and Its Control, in the Treatment of Certain Cases, Amer. J. Psychiat., March, 1929, vol. 8, no. 5.

12. Winkelman, N. W.: Pathological Studies of the Arachnoid Villi and Pacchionian Bodies in Various Types of Convulsive States, A. Research Nerv. & Ment. Dis. Proc., Dec. 28, 1929; The Histology and Pathology of the Pacchionian System with Particular Reference to the Idiopathic and Symptomatic Convulsive States, Arch. Neurol. & Psychiat. **23**:64 (Jan.) 1930.

13. Rowntree, L. G.: Effects on Mammals of Administration of Excessive Quantities of Water, J. Pharmacol. & Exper. Therap. **29**:135 (Oct.) 1926.

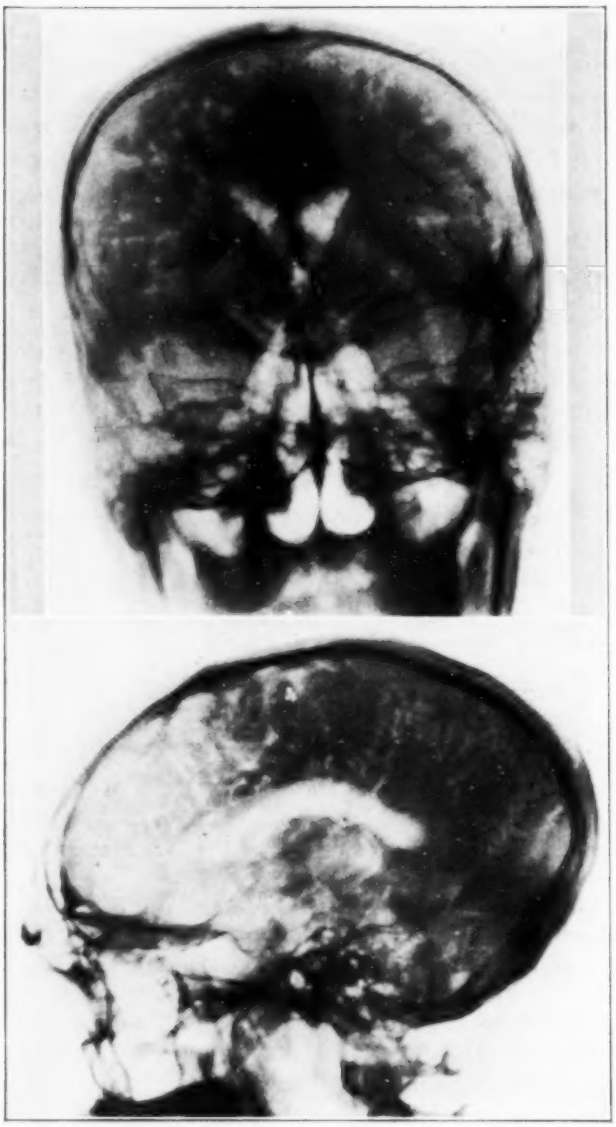

Fig. 1 (I. H.).—Posttraumatic epilepsy with arachnoiditis over the right motor area, verified at operation. Note the areas of atrophy and the increased accumulation of fluid represented by large amounts of air over the frontal lobe, especially on the left side. There is obliteration of the fluid pathways on the right.

Weed [14] not only noted the incidence of convulsive seizures in animals when fluid had been given by the gastric route, but also showed a more rapid onset of seizures in the animal if hypotonic solutions were given by vein. In the work of Ayer [15] on irrigation of the subarachnoid spaces of animals with various solutions, the protocols contained descriptions of convulsive attacks rapidly induced by this method. Weed and McKibben [16] pointed out the swelling of the brain and actual loss of its characteristic markings consequent on the introduction of hypotonic solutions by vein.

Kubie [17] showed similar distortions of the brain with cerebral edema in hydration states, but found that these changes did not occur when the animal was given excessive fluid if free drainage of cerebrospinal fluid was permitted during the period of procedure. Convulsive seizures were common in the undrained animals, whereas the hydrated animals in which spinal drainage was instituted remained symptom-free.

Elsberg and Pike [18] pointed out that when hypotonic solutions had been given intravenously, or when intracranial pressure was increased, convulsive seizures could be produced by approximately one-half the dose of absinthe usually required in the normal animal. On the other hand, if the animal was dehydrated by the use of hypertonic solutions, twice the usual convulsant dose of the drug was required to bring forth an attack.

Drabkin and Shilkret [19] found that convulsions occurred in their animals when large doses of insulin were given, producing hypoglycemic states. If, however, the animals were dehydrated, convulsions did not occur under similar doses.

Drabkin and Ravdin [20] carried this work further and established definitely that the same animal could be used repeatedly to demonstrate this phenomenon, convulsive seizures appearing when the animal was given insulin and allowed free access to fluid, but no convulsive attacks

14. Weed, L. H., and Hughson, W.: Systemic Effects of the Intravenous Injection of Solutions of Various Concentrations with Especial Reference to the Cerebrospinal Fluid, Am. J. Physiol. **58**:53 (Nov.) 1921.

15. Ayer, J. B.: A Pathological Study of Experimental Meningitis from Subarachnoid Inoculation, Monograph, Rockefeller Institute for Medical Research, 1920, vol. 12, p. 26.

16. Weed, L. H., and McKibben, P. S.: Experimental Alteration of Brain Bulk, Am. J. Physiol. **48**:531 (May) 1919.

17. Kubie, L. S.: Intracranial Pressure Changes During Forced Drainage of the Nervous System, Arch. Neurol. & Psychiat. **16**:319 (Sept.) 1926; Brain **51**: 244, 1928.

18. Elsberg, C. A., and Pike, F. H.: Influence of a General Increase or Diminution of Intracranial Pressure upon the Susceptibility of Animals to Convulsive Seizures, Am. J. Physiol. **76**:593 (May) 1926.

19. Drabkin, D. L., and Shilkret, H.: Insulin Anhydremia; Importance of Water-Reservoir in Physiological Crisis, Am. J. Physiol. **83**:141 (Dec.) 1927.

20. Drabkin, D. L., and Ravdin, I. S.: Personal communication to the author.

being produced after the animal had been dehydrated. Their work will be published in full in the near future. The case reported by Howland, Campbell, Matly and Robinson [21] is extremely important in this regard. An epileptic patient with hypoglycemia was found to have an islet cell tumor of the pancreas, removal of which was followed by symptomatic relief and a reestablishment of proper blood sugar values.

The work of Gamble, Ross and Tisdall [22] shows clearly the relation between carbohydrate metabolism and water requirements of the body in terms of storage and mobility. Gamble [23] pointed out the relationship of water storage in the epileptic patient. By determining the fixed base excreted in the urine and that of the "interstitial compartment," he showed that water storage occurs during the interval between attacks, and that this is followed by a definite release of body fluids after the attack. With the appearance of acidosis in children, due to the rapid elimination of the fixed base, dehydration results; his careful experimental and clinical observations seem to establish this point.

The value of the ketogenic diet (Helmholz, Peterman, Barborka, Talbot) is therefore understandable in the light of Gamble's observations and my observations that such a regimen would definitely favor loss of fixed base and consequent loss of fluid volume from the interstitial compartment, the largest reservoir of which is represented by the cerebrospinal fluid. Peterman [24] recently stated that epileptic patients who were placed on the ketogenic diet and rendered free from attacks did not have a return of convulsions when alkalosis was produced, and that hence the ketosis per se was not responsible for the relief obtained.

As Jarloev [25] had assumed that an alkalosis preceded a seizure, the efforts to counteract this shift of the acid-base relation led to the inauguration of the ketogenic diet in the treatment for epilepsy. It now seems evident that the effect of the acid-base relation on fluid metabolism and mobility is probably responsible for the results obtained. Bauer [26] pointed out that of twenty-five infants maintained on a ketogenic diet he had obtained symptomatic relief in approximately 35 per cent. When these same infants were placed on fluid limitation and dehydration for

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21. Howland, G.; Campbell, W. R.; Matly, E. J., and Robinson, W. L.: Dysinsulinism, Convulsions and Coma Due to Islet Cell Tumor of the Pancreas, with Operation and Cure, J. A. M. A. **93**:674 (Aug. 31) 1929.

22. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633 (Oct.) 1923.

23. Gamble, J. L.: Dehydration, New England J. Med. **201**:909 (Nov. 7) 1929.

24. Peterman: Tr. Am. Psychiat. Soc., May 14, 1929.

25. Jarloev, E.: Sur l'équilibre acido-basique du sang humain étudié dans ses rapports avec diverses affections, Compt. rend. Soc. de biol. **84**:156 (Dec.) 1921.

26. Bauer, E. L.: The Management of Epilepsy with Special Reference to Diet, Penn. M. J. **32**:690 (July) 1929.

one year he was able to establish 100 per cent symptomatic relief in his group.

The evidence, both experimental and clinical, becomes more convincing as to the rôle that fluid itself plays in predisposing the patient to a convulsive seizure. Lennox and Cobb [27] stressed the importance of anoxemia in the cycle of the attack as well as the acid-base relationships.

Anoxemia plays a large rôle in determining the permeability of the capillaries (Landis [28]). Alkalosis becomes important, as Gamble has shown it to favor the increase of fixed base ratio and consequent increase in the fluid volume of the interstitial compartment. Forbes and Wolff [29] noted the vascular changes dependent on drugs, sympathetic stimulation and anoxemia by means of a glass window in the skull. The changes which they noted in the size of the vessels, as well as the resultant disturbances in intracranial pressure, must be considered in the light of sudden cerebral insults within a closed cavity that may be augmented by slight transient changes in cerebrospinal fluid volume due to disturbed water metabolism.

In this concept the precipitating factor of the attack might be present but ineffectual under ordinary circumstances, but when the overloading of the cerebrospinal fluid system and tissue spaces with fluid is present, a similar precipitating factor or stimulus becomes greatly augmented. As the cranial cavity reaches its threshold for compensation to rapid changes in circulation, with resultant anoxemia, capillary permeability and tissue edema, pressure changes may become acute.

Weed [30] and Rowntree [31] and Kubie [17] showed clearly the direct relation between the ingestion or intravenous introduction of hypotonic solution and the prompt effect on cerebrospinal fluid volume and pressure, as well as tissue edema and actual gross morphologic changes in the brain resulting from such large quantities.

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27. Lennox, W. G., and Cobb, S.: Epilepsy, Medicine **7**:105 (May) 1928.

28. Landis, E. M.: Micro-Injection Studies of Capillary Permeability: III. The Effect of Lack of Oxygen on the Permeability of the Capillary Wall to Fluid and to the Plasma Proteins, Amer. J. Physiol. **83**:528 (Jan.) 1928.

29. Forbes, H. S., and Wolff, H. G.: Observations of the Pial Circulation During Changes in Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1035 (Nov.) 1928; Cerebral Circulatory Mechanisms: Effect of Hypertonic Solutions, ibid. **20**:73 (July) 1928.

30. Weed, L. H.: Experimental Studies of Intracranial Pressure, A. Research Nerv. & Ment. Dis. Proc., Dec. 28, 1927. Weed, L. H., and Hughson, W.: Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol. **58**: 101 (Nov.) 1921. Weed, L. H., and McKibben, P. S.: Pressure Changes in the Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations, ibid. **48**:512 (May) 1919.

31. Rowntree, L. G.: The Water Balance of the Body, Physiol. Rev. **2**:117, 1922.

In the light of my observations on dehydration in the acute and chronic forms of the convulsive state, there can be no doubt as to the variable influence that fluids may play in predisposing the person to a major attack. The sequence of events surrounding the stimulus and the secondary physiologic response remains to be determined.

One must not overlook such contributing factors as developmental and traumatic disturbances of the cerebrospinal fluid circulating mechanism (Winkelman [12]); the effect on venous drainage and the consequent probable delay in absorption of cerebrospinal fluid, caused by obstructive and congenital lesions of the lateral sinus (Swift [32]) and the jugular veins, as well as obstructive disturbances in circulation as remote as the heart itself (Reisman and Fitz-Hugh [33]). Retention of water, owing to failure of proper kidney elimination, such as is seen in cardiorenal disease, eclampsia, uremia and the acute toxic states, as well as the disturbance in metabolism, especially of carbohydrates, seen in the glandular types, are frequently characterized by convulsive seizures. The secondary effects of these mechanisms on fundamental physiologic processes, such as anoxemia, acid-base relationships and the mechanical factors concerned with circulation, must all be considered when one attempts to view the many conditions encountered throughout the major convulsive state as a whole.

DEHYDRATION

With the clinical experience obtained in the control of acute intracranial pressure [34] in cases of tumor of the brain and cerebral trauma, a method of prolonged dehydration was devised. This method has been applied to the epileptic patient. Thus, if the fluid factors already noted played a significant part in the predisposing of the patient to a major convulsive attack, their regulation and control might indicate the clinical evidence in favor of this view. A program of dehydration was devised for the patient with chronic epilepsy, and a series of observations was begun in June, 1927.

The method employed requires from three to six weeks or longer to establish a basis for fluid balance and to accomplish the desired dehydration (figs. 2 and 3). This necessitates hospitalization under careful check and observation, as the accurate determination of the

32. Swift, G. W.: Epilepsy and Allied Conditions: Mechanical Factors in Their Etiology, Northwest Med. **27**:208 (June) 1928.

33. Reisman, D., and Fitz-Hugh, T. J.: Epilepsia Tarda, Ann. Int. Med. **1**:273 (Nov.) 1927.

34. Drabkin and Ravdin (footnote 20). Elsberg and Pike (footnote 18). Fay, Temple: Administration of Hypertonic Salt Solutions for Relief of Intracranial Pressure, J. A. M. A. **80**:1445 (May 19) 1923; Comparative Values of Magnesium Sulphate and Sodium Chloride for Relief of Intracranial Pressure, ibid. **82**:766 (March 8) 1924; The Control of Intracranial Pressure, ibid. **84**: 1261 (April 25) 1925.

intake and output as well as supervision of the diet cannot at once be left to the patient, no matter how cooperative he is.

During the first week, when the neurologic and routine laboratory studies are being made, the amount of fluid taken daily, a list of the foods comprising the diet and the total urinary output each day are recorded. The patient is instructed to maintain the former routine of fluids and to indulge as freely as has been his custom before admission. A fair estimate of the ratio of intake and output on unrestricted levels is thus obtained, and an idea of the variations of output may be observed. The period of observation is often extended so as to permit the observation of a convulsive seizure. The character of the seizure and the postconvulsive phase are of extreme importance in order to determine later the effect of dehydration and the degree to which it may have to be established.

With the completion of this initial period of observation, an encephalogram is made by withdrawing all of the spinal fluid that can be obtained and by replacing this fluid with air according to the technic described elsewhere.[10] This procedure not only furnishes a clearcut visualization of the brain surfaces for study in the stereoscope, but introduces the stage of dehydration with the cerebrospinal fluid spaces empty, thus gaining what seems to be an important objective early (fig. 2).

After the encephalographic procedure, the patient has a severe headache which persists for one or two days. Liquids and food are not desired by him, and it is here that the restricted fluid level is easiest to establish. The patient is permitted 10, 12 or 16 ounces (295, 354 or 473 cc.) of total liquid in the twenty-four hours, depending on the number and severity of attacks noted in the history. Those with frequent and prolonged attacks of grand mal are placed on 10 ounces of fluid, while those with less frequent attacks and without the stuporous postconvulsive phase may be placed on 12 ounces a day.

It is evident that thirst is the most distressing difficulty encountered until the patient becomes adjusted to this new level. Fluid must be given in small doses, equally divided over the twenty-four hours to relieve this thirst, as the entire amount of fluid would be taken at one time if the opportunity was afforded. White rock, seltzer water, lemon juice and grapefruit juice in measured amounts may be alternated to reduce the feeling of thirst. Water, orange juice and milk can also be given, in doses of from 1 to 2 ounces (29 to 59 cc.), to make up the total for the twenty-four hours. The chewing of orange peel and gum has been found of assistance in some of the younger patients.

In the majority of patients the first ten days of dehydration brings about a definite establishment of the low fluid level without much

further discomfort. Those patients from whom cooperation is obtained for this period usually continue the dehydration under supervision to its most favorable results (fig. 4). In the case of the uncooperative or mentally defective patient, it is almost impossible to control the fluid intake (fig. 5). They will cheat, steal fluid and deceive the nurse or

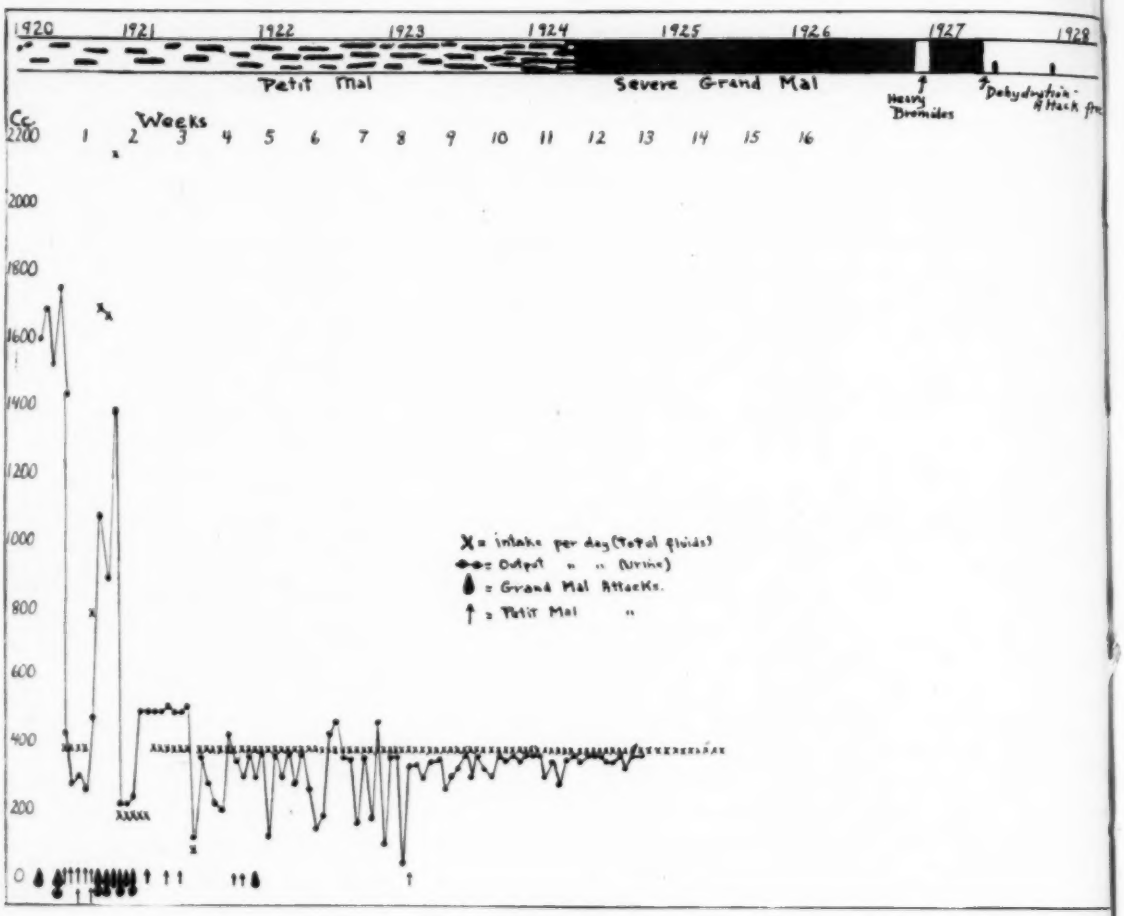

Fig. 2 *A* (W. G.).—Relationship of attacks to intake and output. Initial restriction to 400 cc. of fluid brought about petit mal for the first time in two and one-half years. Unrestricted intake was then followed by a series of grand mal seizures. Limitation of fluid to 400 cc. resulted in disappearance of attacks. Patient has been free from attacks for over two and one-fourth years, with the exception of three instances associated with fluid indiscretions. The longest interval prior to dehydration was six weeks under a heavy dosage of bromide.

attendant. I have found this type of patient drinking from a flower vase, the lavatory, from the hands while washing the face or obtaining the fluid from some source as soon as the opportunity was afforded. The limitations and failures of the method have been greatest in this type, as might be expected.

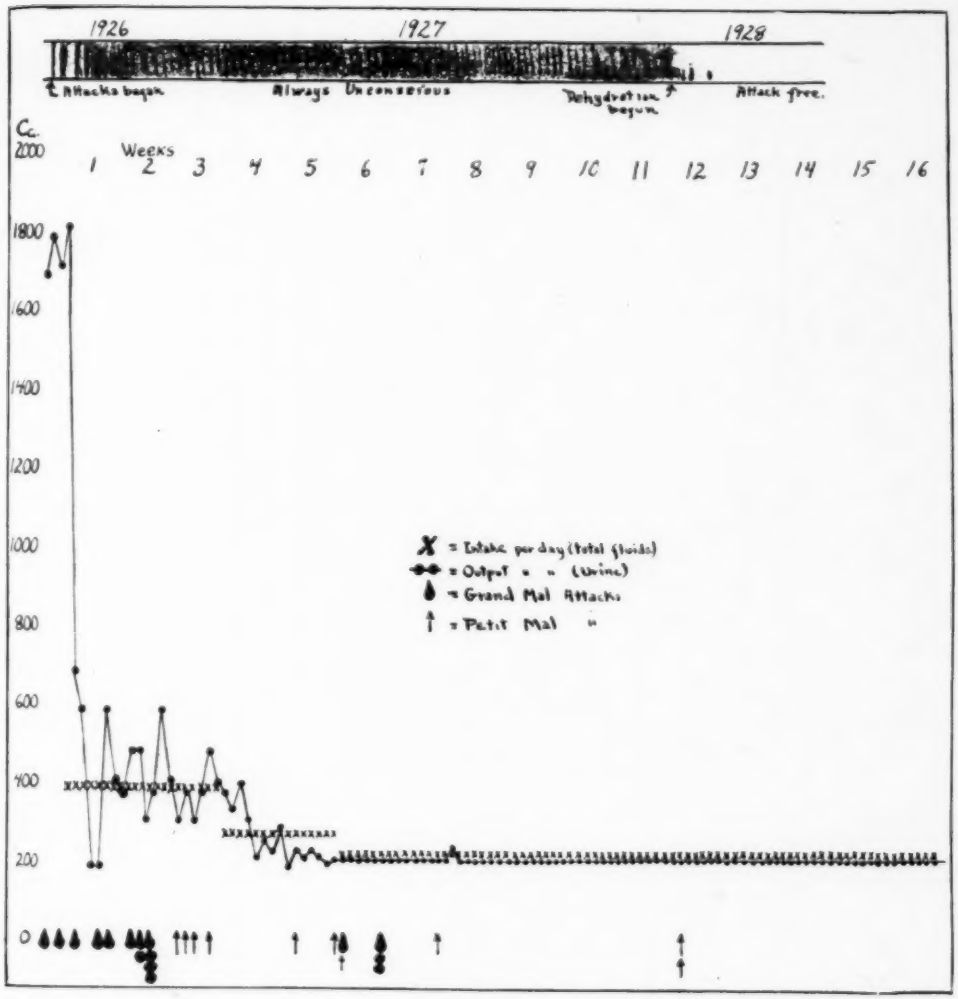

Fig. 2 *B* (E. P., aged 22, with from three to five attacks of grand mal a week, always with loss of consciousness, for two and one-half years; the longest period of freedom had been five or six weeks).—Chart showing intake and output started at 400 cc. with continuation of attacks. The fluid level was reduced to 240 cc. a day before control of the major seizures occurred. Petit mal returned during the first month. A reestablishment of the attacks of grand mal during the menses with two attacks of petit mal at the second period was followed by an attack-free state.

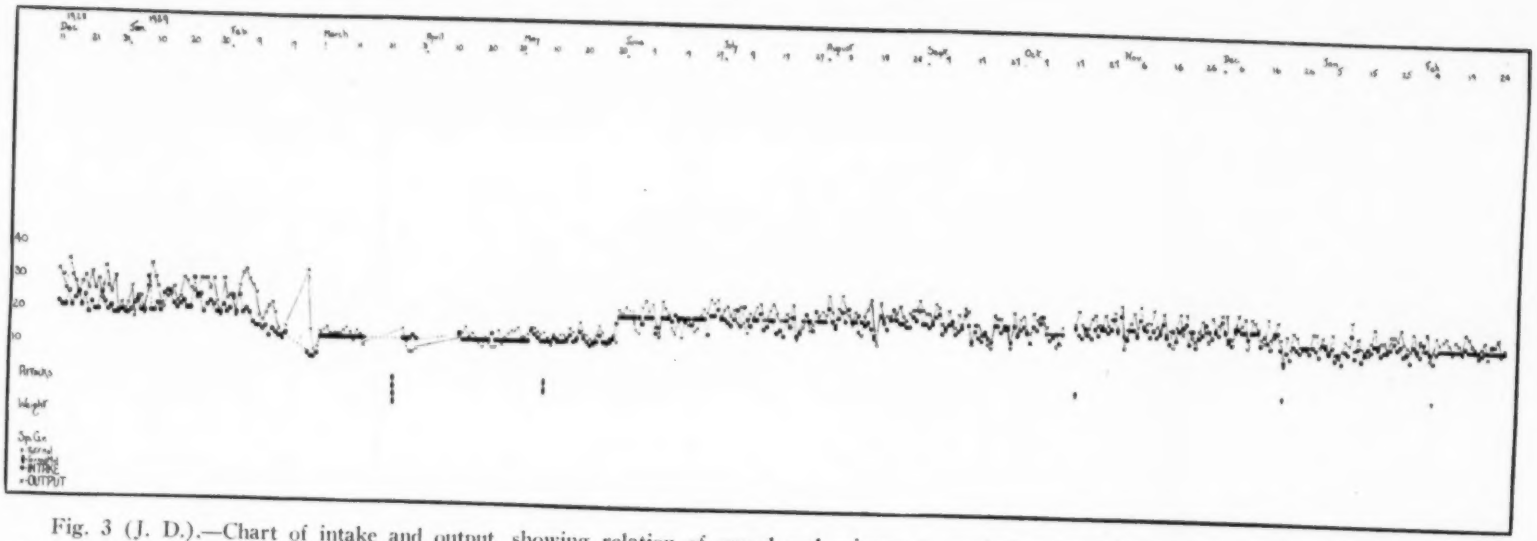

Fig. 3 (J. D.).—Chart of intake and output, showing relation of grand mal seizures to variations in fluid intake. Results of dehydration were obtained only after the patient was placed on strict limitation of fluid to 12 ounces per day. Status epilepticus occurred, followed by restriction of the diet. Two months later, two seizures occurred in association with dietary indiscretions. The patient remained attack free for the next seven months, during which time he worked as a laborer.

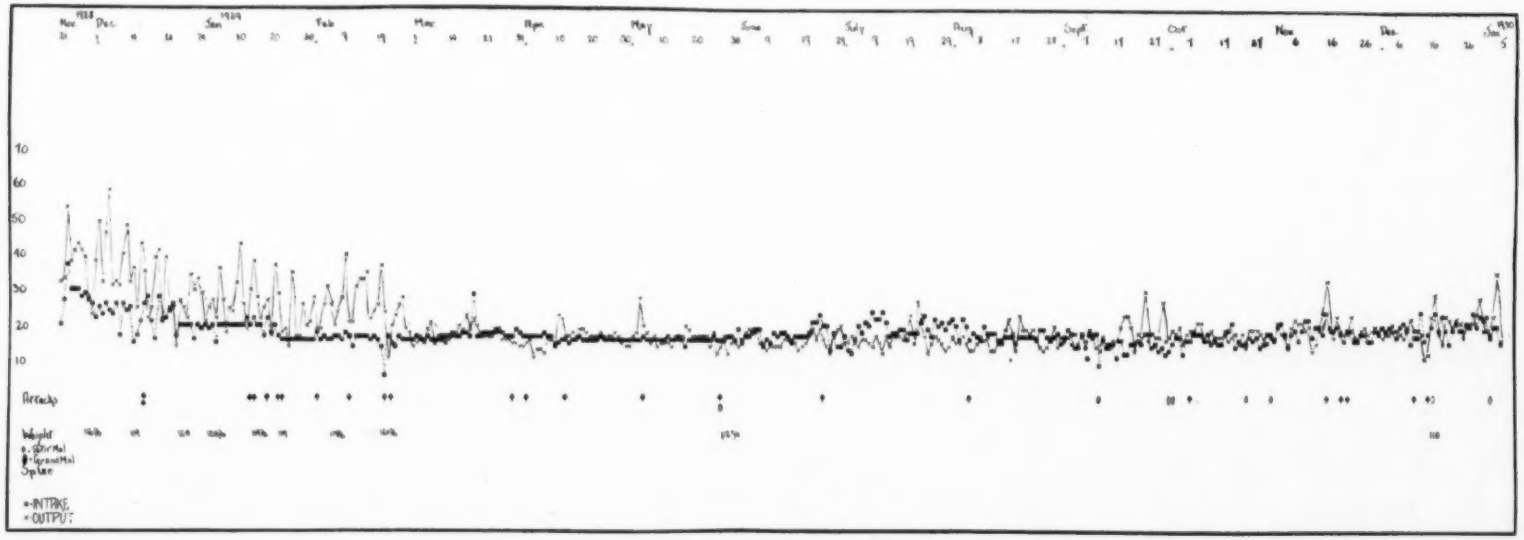

Fig. 4 (G. McC.).—Intake and output chart showing wide variation in intake and output due to an uncontrolled diet. The occurrence of grand mal seizures is indicated at the bottom of the chart. Three months were required to balance the intake and output on a fluid level of 16 ounces a day. During the following four months three seizures occurred, with transient loss of consciousness, and three distinct attacks of petit mal. Increase in fluid, shown at the right of the chart, was followed by slight grand mal seizures. There was operative verification of diffuse arachnoiditis over the left motor parietal area. The patient was able to resume his work. Distinct improvement has occurred up to the time of this report.

By the tenth to fourteenth day after the limitation of fluid, a beginning adjustment of the intake and output levels will be noted (fig. 6). A study of the charts in the cases will indicate this period. At

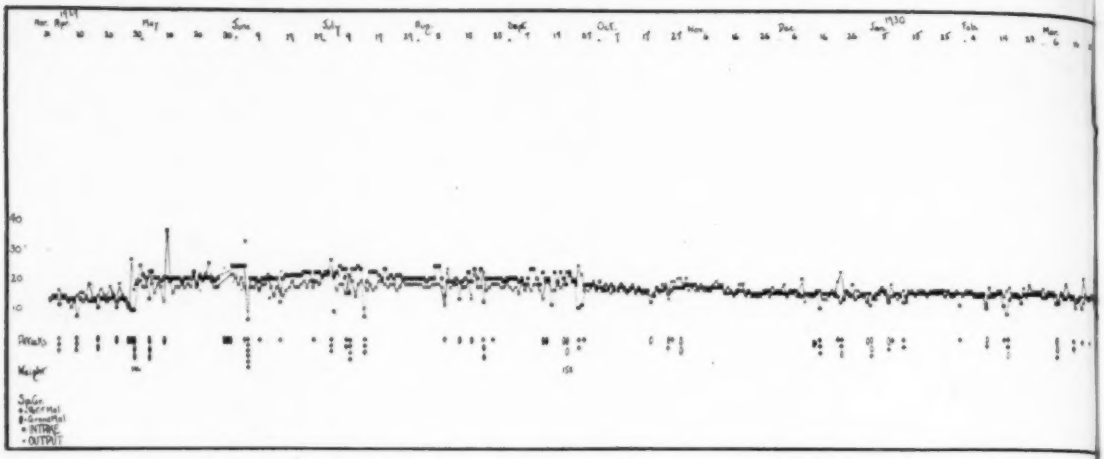

Fig. 5 (F. P.).—The occurrence of grand mal seizures in a case of apparent balance. The patient was slightly subnormal mentally. Frequently, false reports or instances of cheating were found to be responsible for the records submitted. During hospitalization he was attack free on two occasions but was clever enough to submit reports of his own intake and output showing what appeared to be a balance. He was uncooperative and showed only slight improvement.

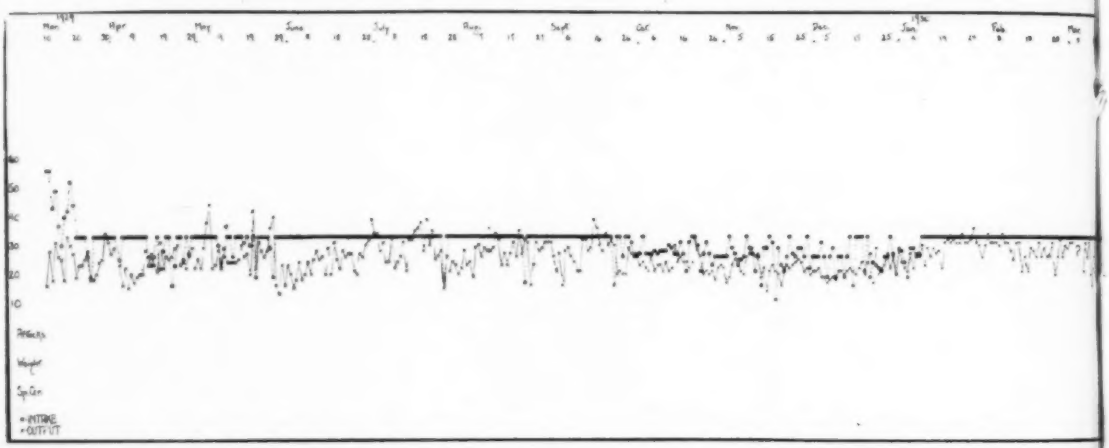

Fig. 6 (B. L.).—An attack-free phase on a 32-ounce balance, showing the relation of output to intake with the widest variation in June when an excessive loss of moisture through the skin gave a period of low output of urine.

this time the output may vary so as to exceed the intake at times, or persist in remaining above the intake (fig. 4). The diet should then be adjusted from the standpoint of its water content. The foods that

are high in water values are curtailed or replaced, and the approach to a drier form of diet is made; toast is given instead of bread, baked potato instead of boiled or mashed and dry cereal with a measured amount of milk or cream instead of cooked forms. The vegetables are drained of juices before serving, and sauces, juicy fruits and gravies avoided.

Ice cream, candy and sweets are not permitted because of the higher water requirements of metabolism demanded by the body for carbohydrates, as shown by Gamble, Ross and Tisdall.[22] The control of the

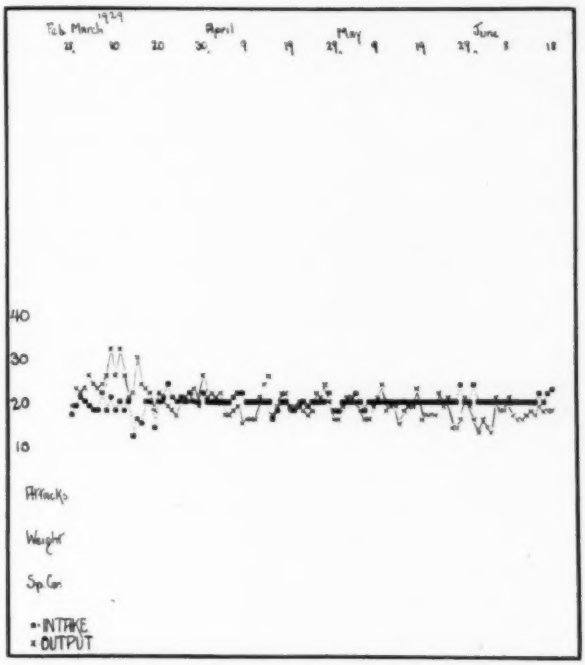

Fig. 7 (C. C.).—This chart shows the close relation between intake and output in a cooperative patient on 20 ounces of liquid a day. Under dehydration the patient has remained free from attacks for one year.

carbohydrate factor has been limited to sweets. Starches have been permitted to avoid acidosis.

A saltless diet has been maintained to assist in the release of body fluids by reducing the amount of the sodium fixed base, shown by Gamble [23] to be responsible for fluid volume in the interstitial compartment (cerebrospinal fluid). The diet is not salt-free, but no salt is allowed to be added to the food, and chipped beef, ham, saltines, etc., are eliminated from the menu. The low salt diet also assists in the control of thirst.

A close balance of intake and output is soon established, and it is at this stage that improvement in the character and duration of the seizures is noted (figs. 2, 3, 4, 6 and 7). It has been the aim to keep the output slightly below the intake. The loss of fluids by skin, breath and bowels cannot be accurately computed; but it has been my feeling that if the intake and output balance, the fluid factors represented in the diet must take care of other losses when the patient reaches a state of balance of intake and output with the weight remaining stationary.

THE THERAPEUTIC EFFECT OF DEHYDRATING EPILEPTIC PATIENTS

In the accompanying tables will be found records of those patients who remained on a definite program of dehydration for two and one-half years.

A survey of the cases and the results obtained indicates that attacks of grand mal have been favorably influenced or controlled in those cases in which true cooperation and balance of intake and output have been accomplished. A return of attacks or their persistence has been found closely associated with fluid indiscretions or imbalances due to dietary excesses.

Several interesting clinical observations have arisen during the two and one-half years of study devoted to dehydrating epileptic patients. It has been rather remarkable that such a close balance of intake and output can be maintained over long periods of time after dehydration has been established (fig. 4). In some cases the total per week showed not more than from 1 to 3 ounces (29.5 to 88.7 cc.) difference between intake and output. A study of the charts in these cases shows such uniformity, in spite of the many variables, that it seems probable that the low level reached represents a balance of the fixed base on a new level, meeting the routine needs of the patient without permitting the former periods of storage for overloads of fluid.

Contrary to what might be expected, the urine of patients continuing on dehydration for a year or more and has shown no evidence of renal irritation. Albumin or casts have not appeared and, aside from a high specific gravity, no changes have been noted due to the low quantity eliminated.

Acidosis has not appeared in a single case of this type of dehydration in this series because the carbohydrate in the diet has been ample. The ketogenic diet has not been necessary in this group, and there is a question as to the safety of combining the two procedures for fear of precipitating a severe acidosis.

The loss of weight is striking during the first three weeks of dehydration, following which the patient maintains a fairly fixed weight level with a slight gradual increase, especially in the growing adolescent group.

TABLE 1.—*Observations on Dehydration of Epileptic Patients During a Period of Two and One-Half Years*

Patient	Sex and Age	Diagnosis	Duration of Attacks, Years	Period of Dehydration, Months	Results of Dehydration: Longest Interval Before	Longest Interval After	Shortest Interval Before	Shortest Interval After	Average per Month: Grand Mal Before	Grand Mal After	Petit Mal Before	Petit Mal After	Comment
E. M.	♂ 12	Posttraumatic epilepsy	2½	30	5-7 days	11 mo.	8-12 hr.	6 mo.	19-25	0.1	0	10-15	Greatly improved; three major attacks in 2½ years; cooperation excellent; attacks with fluid indiscretions
E. M. L.	♂ 19	Idiopathic epilepsy	11	30	2-3 mo.	7 mo.	1-2 days	3 weeks	1-4	0.3	Nocturnal occasional	0	Definite improvement; nine major attacks in 2½ years; cooperation fair
W. G.	♂ 17	Idiopathic epilepsy	5	27	6 weeks	9 mo.	4-6 hr.	3 mo.	12-20	0.14	0	0	Greatly improved; four major attacks in 2¼ years; cooperation good; attacks only with fluid indiscretion
E. P.	♀ 22	Posttraumatic epilepsy (?)	2	26	1 week	21 mo.	4-8 hr.	1 mo.	18-20	0	0	0	Greatly improved; one major attack in 2 years; a few attacks of petit mal during first month of dehydration; good cooperation
E. D. M.	♂ 15	Idiopathic epilepsy (?); postinfectious	7	24	1 mo.	3-5 mo.	2 weeks	1 mo.	2-3	0.25	0	0	Definite improvement; six major attacks in 2 years; on ketogenic diet; cooperation fair
C. C.	♂ 20	Idiopathic epilepsy	¼	22	6 weeks	22 mo.	5 weeks	22 mo.	1	0	0	0	Symptom-free when last seen; no attacks in 1⅝ years; cooperation excellent
E. G.	♀ 15	Idiopathic (jacksonian) epilepsy	1	21	2-3 mo.	5 mo.	10-15 min.	15-20 min.	0	0	200-800 jacksonian	10-100	Unimproved although better at times; mental deficiency; lack of cooperation; plastic arachnoiditis found at operation
R. K.	♂ 8	Idiopathic epilepsy	1	15	1 week	7 mo.	2-6 hr.	7 mo.	7-9	0.07	30-50	0.2	Greatly improved; one attack of grand mal and two or three of petit mal in 1¼ years; attacks with fluid indiscretion; cooperation good
R. S.	♂ 14	Idiopathic epilepsy	14	15 (?)	2-3 days	3 mo.	1 hr.	1 mo.	30-60	?	0	0	Improved; was free from attacks for 3 months; gave up fluid restriction; now on own control; infrequent attacks
G. McC.	♂ 40	Idiopathic epilepsy	5	15	2-3 mo.	2 mo.	12 hr.	4 days	1	0.6	2-5	0.2	Improved slightly; ten attacks of grand mal and three of petit mal in past 15 months; plastic arachnoiditis performed; cooperation excellent
E. W.	♂ 37	Postoperative epilepsy	2	13	1 mo.	7 mo.	6 hr.	2 weeks	1-4	0.5	0	0	Improved; free from attacks for past 7 months; cooperation fair at first, excellent now
H. R.	♂ 12	Idiopathic epilepsy	3	12	3 weeks	2½ mo.	8-10 daily	1-2 daily	100-150	9-15	0	10-30	Improved slightly; control not possible; cooperation poor
K. D.	♀ 17	Idiopathic epilepsy	16	1½	10 days	6 weeks	6-12 hr.	6 weeks	20-30	10-20	0	0	Unimproved; mental defective; free from attacks during dehydration; allowed to return to former fluids; no cooperation
R. D.	♀ 22	Idiopathic epilepsy	4	1	1 mo.	1 mo.	6-8 days	8-10 days	3-7	3-7	0	0	Unimproved; free from attacks during study; returned to institution; no supervision; mental deflective; no cooperation

TABLE 2.—*Observations on Dehydration of Epileptic Patients During a Period of Less Than One Year*

Patient	Sex and Age	Diagnosis	Duration of Attacks, Years	Period of Dehydration, Months	Results of Dehydration: Longest Interval, Before	Longest Interval, After	Shortest Interval, Before	Shortest Interval, After	Average per Month: Grand Mal, Before	Grand Mal, After	Petit Mal, Before	Petit Mal, After	Comment
E. P.	♂ 17	Idiopathic epilepsy	2	12	1 mo.	5 weeks	4 hr.	4 hr.	10-12	1-3	0	1-2	Slight improvement; uncontrolled false reports; cooperation poor; mental defective
J. D.	♂ 25	Idiopathic epilepsy	6	9	1 mo.	5 mo.	4 hr.	1 week	1-4	0.6	0	0	Great improvement; attack-free; two seizures in past 10 months; cooperation excellent
M. G.	♀ 20	Idiopathic epilepsy	15	7	5 weeks	3 weeks	8 hr.	1 day	4	4	150	20-30	Unimproved; cooperation excellent; fewer attacks of petit mal
B. L.	♀ 22	Idiopathic epilepsy	6	7	1 year	Attack-free	5 days	Attack-free	0.18	0	0	0	Free from attacks from beginning of dehydration; cooperation good
C. L.	♂ 30	Posttraumatic epilepsy	4	6	5 mo.	6 mo.	12 hr.	6 mo.	0.5	0	1-2	0	Free from attacks; cooperation good
A. F.	♀ 6	Idiopathic epilepsy	2½	6	1-3 days	4 mo.	Status	4 mo.	10-30	0.3	30-50	0	Greatly improved; two attacks with tonsillitis; cooperation good
E. W.	♀ 12	Idiopathic epilepsy	3	6	1 week	1 mo.	1 hour	2 weeks	0	1	15-20	0	Attacks of petit mal ceased; attacks of grand mal once a month; cooperation good
A. O'N.	♀ 23	Posttraumatic epilepsy	20	6	3 weeks	2 mo.	Status	1 mo.	2	1	0	0	Slightly improved; mental defective; cooperation poor

A lessening of irritability and an improvement in memory and mental alertness during the early stages of dehydration have been outstanding changes noted by the epileptic patient and those associated with him.

The change in the character of the seizure has been variable in the group as a whole. The most common early improvement has been a lessening of the duration of the attack, with freedom from the stuporous or sleeping phase immediately following the convulsion. There has been a rapid return to consciousness following the attack, and when vomiting and headache have occurred, these symptoms have disappeared early in the course of dehydration.

In some cases (E. M., E. P., and G. McC.) the grand mal seizures have receded into petit mal. In others (W. G., C. C., J. D., and C. L.) both grand mal and petit mal types have been controlled by proper balance.

When petit mal has replaced grand mal, all efforts at dehydration have so far failed to affect the minor seizures (fig. 8).

The distinct impression has been gained in certain cases (W. G., E. G., and R. K.) in which withdrawal of fluids has been followed by petit mal and the giving of unrestricted or forced fluids by grand mal that fluids have been responsible for predisposing the cerebral centers to a generalized explosion and convulsive attack with loss of consciousness, whereas limitation of fluids tends to focalize the attack or produce transient phases of psychic arrest such as one sees in petit mal. Generalized convulsions, loss of consciousness with falling, stupor and post-epileptic sleep have disappeared in all but one case (E. P.).

In one case (E. W.), petit mal has been replaced by grand mal, but as one grand mal seizure occurred before starting the treatment, it is a question as to whether the patient was not in that stage of transition between the minor and major forms of the attacks and that what remains are occasional grand mal seizures not yet entirely controlled.

The relationship between return of attacks and fluid indiscretions is striking and is best illustrated by the case of W. G. (fig. 2).

A boy, aged 17, had had from twelve to twenty attacks of grand mal a month for five years. He was kept at home and received his education through private tutors. The longest interval of freedom from attacks had been six weeks under heavy doses of bromides, several months prior to his undertaking dehydration. At one sanatorium he had been given colonic irrigations and a status epilepticus had promptly developed which lasted for several days. The first two weeks of dehydration changed the major attacks to minor seizures, and at the end of one month he returned home free from attacks. Two months passed without a seizure when he was placed on a total fluid intake of 16 ounces per day. On Thanksgiving Day, his family held a celebration over this long period of relief. On this occasion the patient broke his fluid and dietary restrictions. The next day a series of convulsions occurred. He was sent to the hospital, his spinal canal was drained, magnesium sulphate was given by mouth, and he was again placed on 12 ounces

of fluid. Six months of freedom from attacks followed until an illness with influenza required, in the judgment of the attending physician, an increase in his fluid intake. Several attacks occurred during the ten days of illness. Another five months of freedom followed until the next Thanksgiving Day. At this time the parents were careful about diet and fluid, but the boy had entered college in the fall, played on the school band, was vice president of a club and led his class in English. His return home on a vacation led to his renewing friendships with his former associates, and on Thanksgiving evening he indulged in some soda "pop"

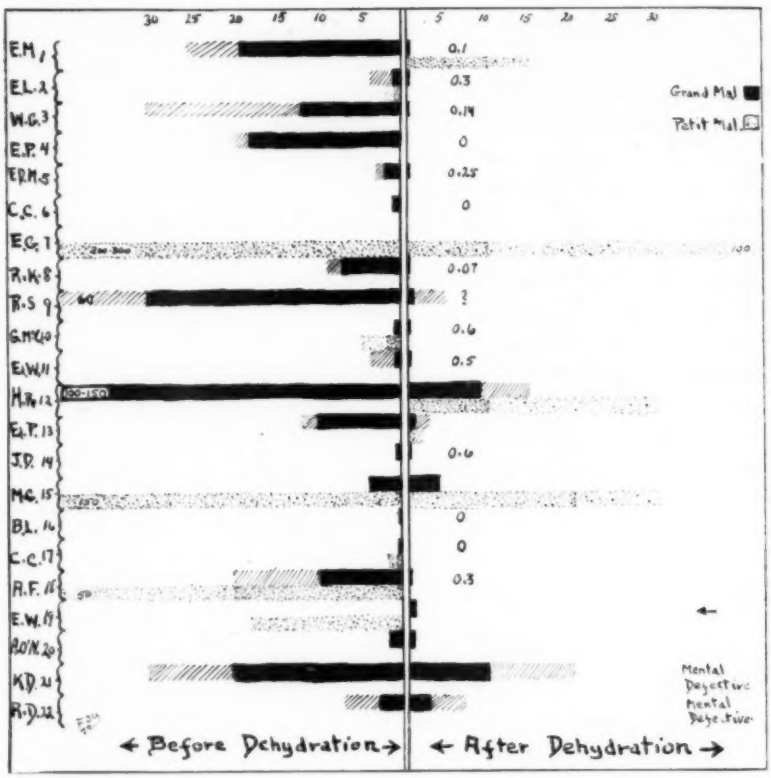

Fig. 8.—Graphic representation of the effect of dehydrating epileptic patients on the relative number of attacks per month (taken from tables 1 and 2).

and two glasses of malted milk. Status epilepticus developed that night, and several attacks followed on the next day. He began the dehydration again and finished the school year with credit. No attacks occurred until the summer vacation (1929), when he took a 4,000 mile automobile trip with another boy, and the wayside "hot dog stand" overcame his habits of regulation. An attack occurred during this trip. To the time he was last seen there had been no recurrences.

The case is cited because it is so filled with the human factor as to how far the patient could control his desire to partake in the unrestricted life about him. The change from a "shut-in" type to full activity was

a remarkable advance in his state. The close relationship between fluid and dietary indiscretions and his attacks were definite, as they have been in many other cases studied.

The fact that limitation of fluid is only a controlling influence is undoubted, and that the underlying cause for the attack remains to be found is certain. At best, fluid can be considered only as a predisposing or contributing factor to the mechanism of the attack. Like diabetes before the advent of insulin, favorable results have been possible only when strict regulation of the diet has been carried out; with even slight deviation from the prescribed regulation, the symptoms recur. The fundamental pathologic process and abnormal mechanism remains unaffected.

K. D., a girl, aged 17, illustrated the futility of dehydration when mental deficiency was present. For sixteen years she had suffered from attacks of grand mal, averaging from twenty to thirty a month. She was bedfast at home under a nurse's charge. For eight years, the nurse or mother could not recall a period of longer than ten days when she had been free from attacks. Contractures had developed in the legs. There was marked mental deficiency. She could read, but otherwise had the mental age of 6.

She was placed on 8 ounces (236 cc.) of total fluid intake per day, and was free from attacks for six weeks. During this time she became brighter, got out of bed and with the aid of braces walked about the house. She joined the family at meals, where she was unruly and quarrelsome and became a definite behavior problem. She was taken to the theater as a novel diversion. Here she exposed herself in public, made advances to men and created a scene on the streets. She had to be watched continually. She would run outdoors and approach men on the streets near her home. In order to prevent a public scandal, the parents deciding that the behavior she showed was worse than the former epileptic attacks, abandoned fluid limitation. Thirty-six hours later, she had a series of attacks that were far worse than any they had seen. These lasted for four days. She returned to the dull, apathetic state, with frequent attacks, and when last seen was unimproved.

This case serves to illustrate several similar ones in which I have found that a release from the convulsive state in the mentally defective group permits a behavior problem to develop which is even worse. What residual mental activity the patient possesses is released into a wider field of social disturbance.

The outlook in this type of case is hopeless in my opinion, for invariably the encephalographic studies have shown widespread areas of atrophy of the brain in the frontoparietal regions of the cortex. The mechanism of the production of this atrophy, as I have come to view it, is taken up in a series of papers[35] published elsewhere, in

35. Fay, T., and Winkelman, N. W.: Widespread Pressure Atrophy of the Brain and Its Probable Relation to the Function of the Pacchionian Bodies, and the Cerebrospinal Fluid Circulation, Am. J. Psychiat. **9**:667-686 (Jan.) 1930. Fay, T.: Generalized Pressure Atrophy of the Brain, Secondary to Traumatic and Pathologic Involvement of the Pacchionian Bodies, J. A. M. A. **94**:245 (Jan. 25) 1930. Winkelman (footnote 12).

which the factors involved in the production of chronic intracranial pressure by some obstructive lesion producing increase in subarachnoid fluid act according to the laws of hydraulics within a closed system, producing pressure atrophy, due to the hydraulic "cast" characteristically confined to certain areas of the brain alone.

An example of the care required in searching for disturbance in fluid balance when intake of fluid and diet has been controlled is illustrated in the case of E. W. Periodically the return of attacks associated with increase of output finally disclosed that an enema of 1 quart (946 cc.) of water was used for constipation. This corresponded to the increase in fluid noted after these enemas, the correction of which resulted in the patient's remaining free from attacks for eighteen months.

Two interesting cases have come under my observation, though records of intake and output were unobtainable because the patients lived at a distance and remained under the care of the referring physicians. In each case a colectomy had been done, three and five years previously, with the idea of removing "the intestinal toxic cause for the attacks." Both patients had had fluid bowel movements since the operation. The attacks had been lessened, but recurred at longer intervals. The patients were instructed to reduce the fluid intake to a minimum. The effect of fluid reduction first noted was that the stools became formed. Later reports from both patients showed improvement in the number of attacks and greater intervals between them on this fluid limitation alone. The interesting part that the colon may play in fluid absorption seems indicated in both cases. The claims of benefit from the colectomy that are justified may be due to the cutting down of the absorbing area for fluids ingested (diarrhea) in such a way as to produce a partial dehydration in this manner.

COMMENT

The clinical confirmation that has recently come from various observers (Bauer, Strecker, McQuarrie [36]) using this method has given definite assurance that its application has been of extreme value in the control of the major form of the convulsive state in many infants, children and adults. Our series includes a representative cross-section of the chronic convulsive group.

In the acute convulsive states often associated with such conditions as eclampsia, uremia and infections of childhood, spinal drainage with

36. McQuarrie, I.: Epilepsy in Children, the Relationships of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

proper regard to fluid limitation, balance and dehydration has brought prompt relief from the generalized seizures and stupor encountered in these hydration states.

In my experience, cerebral hydration states have been constantly found whenever major convulsive seizures have been present. In seeking the common denominator running throughout the major convulsive state, some form of fluid imbalance or disturbance in water metabolism could be traced in almost every instance. Frequently the causes lay outside the cranial cavity, although their indirect effect on water metabolism and supracortical edema was evident when considered in the light of the experimental and physiologic factors noted earlier in this paper.

A grouping of the cases around the structures influencing water metabolism and mobility led to the construction of figure 9. Irrespective of the pathologic condition when generalized convulsions were present, the coincident factor was a cerebral hydration state, either acute or chronic.

When one considers that a normal human being can develop a generalized convulsion if the fluid intake is sufficiently forced and the kidneys are "shut down" (eclampsia), following trauma (cerebral edema), or simply by forcing large quantities of fluids (two cases observed by me), the important effect of the fluid itself cannot but command attention. When acute or chronic major seizures can be controlled at will over a period of two and one-half years by limitation of fluid intake in the chronic forms of the convulsive state, it seems justifiable to assume that this daily fluid variable plays the predisposing part in the cycle of events.

The factors that may disturb the usual relation of water to tissue fluids and the "interstitial compartment" (Gamble) have been enumerated in figure 9. Compensation for water storage or its elimination by the body may, in the presence of one or more of these factors, be such that only unusual overloads will affect the structures involved (cortical motor surfaces), or conditions may be such that even a moderate consumption of fluid is not tolerated. Thus, the varying intervals have seemed directly proportional to this factor.

The major convulsive state may be found associated with the following factors concerned with disturbance of water metabolism, supracortical cerebrospinal fluid accumulations and mobility (fig. 9):

1. Cortical lesions situated in the frontoparietal areas of the brain, such as postinflammatory arachnoiditis, scars, tumors of the brain and traumatic defects (Weed, Bagley, Winkelman, Cushing).

2. The pacchionian bodies responsible for proper filtration and reabsorption of spinal fluid impaired by hyperplasia, aplasia, fibrosis and calcification seen in obstructions due to inflammatory exudates, birth injuries, subarachnoid hemorrhage, senile calcifications and anomalous or improper developments (Weed, Winkelman).

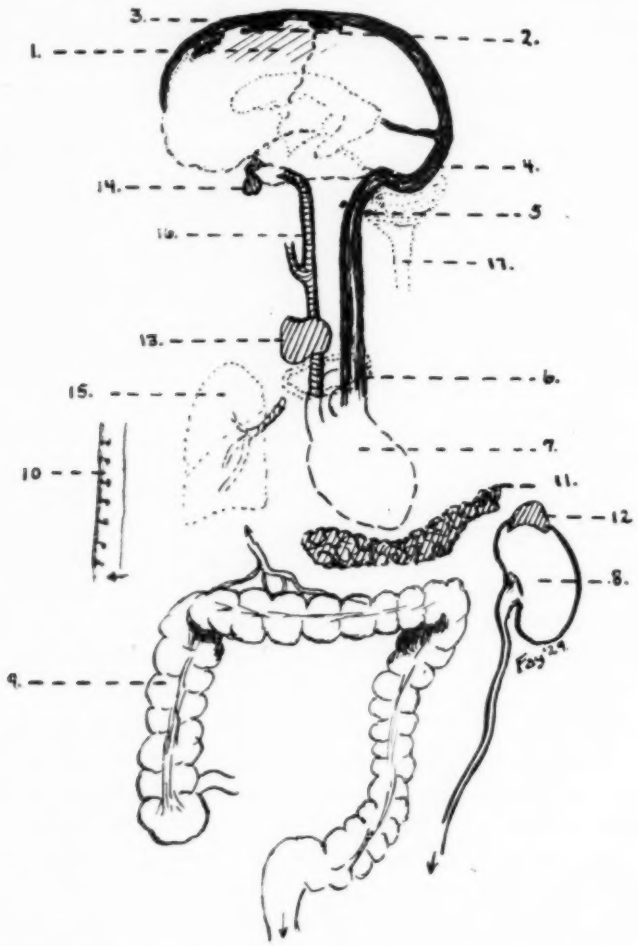

Fig. 9.—Contributing factors that may influence cerebrospinal fluid volume and pressure frequently found in various types of the acute and chronic major convulsive states.

3. The longitudinal sinus subject to birth injuries, thrombosis and venous stasis (Winkelman, Swift).

4. The lateral sinuses and the sigmoid, frequently the site of congenital anomalies. The extension of inflammation from the mastoid, such as thrombosis (Swift).

5. The bony openings of the jugular foramen; stenosis, asymmetry and anomalies in unilateral development frequently found in patients with idiopathic epilepsy (Swift, Fay and Pendergrass).

6. Venous obstruction, due to an enlarged thymus gland within the fixed first thoracic ring, with passive cerebral congestion and stasis (Fay, Pendergrass).

7. Foreign bodies in the esophagus (two cases, Chevalier Jackson); metastatic carcinoma of the neck (one case, H. K. Pancoast); tonsillar inflammations and abscesses, cardiac lesions producing passive congestion, abnormalities of the heart, (patulous interventricular septum, one case), Stokes-Adams' disease; terminal states seen in cardiorenal insufficiency (Reisman and Fitz-Hugh et al.).

8. Acute and chronic involvement of the kidney associated with conditions of inadequacies, such as eclampsia, uremia and acute toxic infections especially in childhood.

9. The colon, representing the largest area of fluid absorption and concentration of fluid fecal contents (two cases cited in this paper), as a regulating fluid factor with cycles of constipation in the light of desiccated stools so frequently associated with attacks of epilepsy.

10. Skin elimination in its relation to fluid volume, especially when hyperthermia reduces the function of this factor in fluid limitation and water balance causing retention; acute toxemias and climatic influences.

11. Pancreatic function in regard to insulin and carbohydrate metabolism; water storage due to carbohydrate metabolism (Gamble, Ross and Tisdall); hypoglycemia in relation to attacks (Howland, Campbell, Matly and Robinson); insulin in relation to hydration and dehydration (Drabkin and Shilkret, Drabkin and Ravdin).

12. Suprarenal interrelation with insulin and carbohydrate metabolism undetermined.

13. Thyroid mechanical pressure on the jugular veins, when substernal and enlarged, and its interrelation with metabolism and oxygen utilization.

14. Pituitary interrelation with metabolism and other glandular structures; effects of pituitrin on the vasomotor system in relation to renal output and the consequent production of attacks (Fremont-Smith, McQuarrie).

15. Intrapulmonary structures and factors concerned with respirations; intrathoracic pressure or pulmonary congestion; hyperventilation (Rosett); anoxemia and the resultant physiologic changes due to this factor (Landis, Lennox, Lennox and Cobb).

16. Carotid circulation in terms of cerebral blood volume, blood pressure and vasomotor responses (Kussmaul and Tenner, Forbes and Wolff).

17. Medullary centers and their control of peripheral vasomotor responses, both cerebral and splanchnic, in terms of the resultant blood pressure, anemia and anoxemia and the physiologic cycle produced by such changes.

When the entire convulsive state, either acute or chronic, is considered in the light of these contributing factors influencing water metabolism and mobility, with its variable secondary effect on cerebrospinal fluid volume and pressure, it is possible to classify the many so-called varieties of convulsive conditions under a common denominator, such as water metabolism.

It has seemed evident to me that the fluid itself is in no way the cause of the convulsive seizure. Apparently, its rôle has been to predispose the motor level to a state in which the necessary stimulus has found a widespread area free from inhibitory control, permitting a generalized response. This has become a necessary concept as our observations have accumulated on the gradual receding of the major attacks so as to involve less and less of the motor system as dehydration becomes established.

Finally, when dehydration has been well established, the general seizures disappear or become so focal that the stimulus does not involve more than a small area, so that there remain only jacksonian attacks without the loss of consciousness or bilateral manifestations.

The vasomotor factor coincident with the attack may play a rôle in the actual precipitation of the cycle of events surrounding the physiology of the problem, but I believe that this factor requires the predisposing increase in supracortical fluid to become effectual in giving rise to a generalized seizure.

Whether a simple stimulus (central or peripheral) finds a prepared motor threshold at a certain moment, or whether it produces a vasomotor response augmented by the hydration factor remains for the physiologist to determine.

The fact that one is now able to produce or control major seizures almost at will through the factors surrounding water metabolism indicates that one is dealing with a symptom-complex and that generalized convulsive seizures with unconsciousness and stupor are a superadded phenomenon related to certain phases of intracranial hydraulics and pressure which have nothing to do with the true origin of the stimulus or its response. It may merely determine the spread and degree of effectivity.[37]

It is evident from such a concept that the rational treatment for generalized convulsive seizures lies in the fullest correction of the underlying factors concerned in the patient's fluid imbalance. The readjustment of the deficiency may or may not be possible, but the care exercised in establishing or maintaining the proper threshold for fluid metabolism in the presence of such factors will indicate the proper measures and best results to be obtained by fluid limitation and dehydration.

I have demonstrated that it has been possible to remove or diminish the major form of the convulsive state in every case in which a true balance of fluids has been obtained and that this control has been possible in some instances for a period of two and one-half years. There

37. These considerations have been taken up in detail elsewhere (Fay, T.: Epilepsy: Clinical Observations on the Control of Convulsive Seizures by Means of Dehydration, J. Nerv. & Ment. Dis. (May) 1930.

has been a return of the major seizures whenever indiscretions or storage of fluid has occurred, indicating that no permanent benefit can be expected from this method. At best it is a rational control of the major attacks and may place the symptom-complex in the same category as diabetes mellitus, in which symptomatic relief is possible as long as the patient adheres to the proper routine.

CONCLUSIONS

Proper control of fluid intake, combined with dehydration, has greatly diminished the tendency to convulsive seizures in certain cases representing various types of epilepsy.

Two and one-half years of observations on a group of patients under dehydration treatment has led to the distinct impression that fluid plays an important part in predisposing the patient to a convulsive seizure.

The "generalized" and "stuporous" phases of the attack have been relieved by dehydration; this may indicate that increased amounts of supracortical fluid under specific conditions [37] predispose the patient to a widespread effect of the precipitating stimulus responsible for the attack, and that major convulsive seizures are in reality a superadded phenomenon not necessarily related to the basic disturbance.

Dehydration has proved to be a valuable adjunct in the control of major convulsive seizures and has been found to be effective when other means of treatment have failed. The difficulty lies chiefly in maintaining a strict regulation of fluid intake and in obtaining continued cooperation on the part of the patient. Those who have obtained a proper balance have been free from the major form of seizures during long periods when this method of control has been maintained.

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INTERPRETATION OF ENCEPHALOGRAPHIC OBSERVATIONS

COMMENTS ON THOSE FOUND IN THE CONVULSIVE STATE*

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Encephalography is a procedure in which a series of properly exposed roentgenograms are made of the head in several positions in the erect posture within one hour following the removal of all the available cerebrospinal fluid and its replacement with air by the cisternal or lumbar route.

Dandy (1918-1919) was the first to visualize the possibilities of this method, as well as to demonstrate the cerebral ventricles by the direct introduction of air into them. Bingel (1921-1923) pointed out the value of injections of air by the lumbar route. At about the same time, Martin and Uhler (1922) reported a series of cases in which this method had been of diagnostic value. Since the inception of encephalography many investigators have confirmed its value as a diagnostic procedure in establishing the character, localization and extent of cerebral lesions.

TECHNIC

The success of this procedure depends on the cooperation of neurologist, neurosurgeon and roentgenologist. The neurologist or neurosurgeon must drain off all the available spinal fluid, and the roentgenologist must make technically perfect roentgenograms. Pancoast and Fay (1929) outlined the following procedures with regard to the surgical preparation of the patient.

1. The patient is placed on a litter in a lateral horizontal position. A gold or nickeloid needle is inserted into the space between the fourth and fifth lumbar vertebrae. When clear, colorless spinal fluid is encountered, a pressure reading is made at the beginning of the procedure. A second needle is introduced into the space between the third and fourth lumbar vertebrae. After clear spinal fluid is obtained from this puncture, the manometer is disconnected and the stylets of the needles are replaced. The patient is placed in the erect posture, great care being observed in maintaining the same relative curvature of the spine in order

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* From the Department of Roentgenology, Hospital of the University of Pennsylvania. The interpretation of the roentgenograms was made possible largely through the aid of the D. J. McCarthy Foundation for the Study of Nervous and Mental Diseases, University of Pennsylvania.

that the needles may not be disturbed. The normal pressure of the spinal fluid in the horizontal position is approximately 8 mm. of mercury, and in the adult the normal pressure in the sitting position is 20 mm. of mercury.

2. A manometer is connected to the upper needle to allow a constant reading throughout the entire procedure of drainage and replacement. The canal is drained through the lower needle. If the pressure is 20 mm. of mercury when the procedure begins, the spinal fluid is allowed to drain into a graduate from the lower needle until the pressure becomes 10 mm. Then a syringe of air is connected to the lower needle and the air is introduced slowly until the pressure rises to 20 mm. This procedure is repeated until all of the fluid has been removed. It should be noted that the removal of fluid and the replacement with air is a pressure per pressure mechanism rather than a volume per volume. Air expands at body temperature, and every effort is made to maintain the pressure that was present at the beginning of the procedure. It has not been found necessary to take any precaution in the selection of the air to be used, ordinary air in the room being introduced into the spinal canal.

3. Fluid should never be sucked out of the canal but should be allowed to drain. During the drainage an assistant rotates the head from side to side and from back to front as far as possible, taking care not to change the axis of the spinal canal. This rotation is most important, as on this procedure depends success or failure in draining the lateral ventricles. A satisfactory injection of air requires the withdrawal of at least from 100 to 125 cc. of fluid in a normal adult. In my hands adequate drainage of the cerebrospinal fluid by the cisternal route has not been possible, probably owing to the danger of manipulation of the head with the needle in situ.

4. After the canal has been drained the patient is placed in a wheel chair and taken to the roentgen department for examination. The head is maintained in the erect posture in a midline position so as not to allow any distortion from air seeking the highest point and from possible residual fluid in the ventricle seeking the lowest point.

The following symptoms usually are noted in patients. After the introduction of about 40 cc. of air, the patients develop severe frontal headache. This is an indication that air has reached the subarachnoid spaces over the frontal lobe. Following this, profuse sweating usually occurs. During the rotation of the head and the emptying of the ventricles, vomiting may ensue. Slowing of the pulse may be encountered, and a pulse rate of 60 beats per minute is not uncommon. The headache is the disturbing factor to the patient. Chloral hydrate, 15 grains (0.97 Gm.) is given to the patient one hour before the procedure, to reduce the intensity of the pain. The headache is intense for from six to eight hours, and is present in a slight degree for from twenty-four to thirty-six hours.

Roentgen Technic.—In a previous paper (1928), I described the apparatus and technic employed in this procedure. The essential feature of the method is the use of a vertically placed, flat Bucky diaphragm, as all films must be made in the erect posture and the roentgenograms should be technically perfect, with the maximum amount of contrast. Roentgenograms made without the aid of the Bucky diaphragm are useless in this procedure, except in showing the ventricles. Finer details of the subarachnoid markings are lost or are so indefinite as to make interpretation difficult. Technically perfect roentgenograms imply the proper technic on the part of both the neurologist or neurosurgeon and the roentgenologist. Sufficient air must be introduced into the spinal canal, and it must be distributed properly by proper manipulation of the head, or incorrect conclusions may be drawn.

After the fluid has been withdrawn and the air introduced, the patient is brought to the roentgen department and placed in a chair that has large casters on it so as to facilitate moving of the patient. Seven roentgenograms are made: lateral stereoscopic views of each side, stereoscopic views in the anteroposterior direction and one postero-anterior view. The stereoscopic shift for the lateral views are in a horizontal direction in order to prevent a distortion of the basal cisternae by superimposing the base of the skull. The anteroposterior roentgenograms are made by a vertical shift in order that there may be no shift of the midline structures. When the lateral views are made, the head is held tightly by

Fig. 1.—Fixation of the head for the lateral stereoscopic views. A horizontal shift of 5 inches (12.7 cm.) is used.

a restraining band (fig. 1); when the anteroposterior view is made, the chin is flexed on the chest in order that the frontal sinuses are not projected over the air-containing third and fourth ventricles; otherwise they will be difficult to interpret (fig. 2). It is absolutely essential that the head be properly placed in both the lateral and the anteroposterior directions; otherwise confusing distortions of the ventricles will be found on the roentgenograms (fig. 3).

The factors used in making the roentgenograms are as follows:

Fixed target film distance of 44 inches (111.7 cm.). This will allow plenty of room to manipulate the patient. The roentgen rays are approximately parallel, thereby causing a minimum of distortion.

The stereoscopic shift is 5 inches (12.7 cm.); kilovoltage, 100; milliamperage, 20; time for lateral views, from six to eight seconds; time for anteroposterior views, from eight to ten seconds.

In children and infants, when they are under an anesthetic and it is imperative to obtain quick exposures, the factors are: kilovoltage, 88; milliamperage, 100; time, from 2 to 3 seconds for each view.

The Bucky diaphragm is placed in a vertical position on a special stand which allows it to be lowered or raised for various heights, and it can be angled in any position.

Fig. 2.—The chin is fixed on the chest and maintained by the restraining band. Note the position of the tube for the first exposure in the anteroposterior view.

INDICATIONS

The indications for encephalography include cases in which the symptoms are obscure, such as those following trauma, inflammation and senility, epilepsy, hemorrhage, tumors of the brain, hemiplegia and birth injuries. As encephalography is the replacement of spinal fluid by air introduced into the subarachnoid spaces surrounding the brain and within its ventricles, it is evident that encephalography is indicated in any condition of the brain or its surrounding structures that would distort

or obliterate the subarachnoid fluid pathways. Many of these conditions cause few or obscured symptoms, and much information of importance has been obtained from employing this method.

CONTRAINDICATIONS

The procedure is contraindicated in all patients having a pressure of 20 mm. of mercury or over in the horizontal lateral position. Lumbar

Fig. 3.—The patient is in position for the postero-anterior view.

puncture in such persons may cause a foraminal hernia of the posterior cerebellar hemispheres. Any obstruction of the ventricular system in the region of the third ventricle, aqueduct of Sylvius and the fourth ventricle, such as is found in tumors in any of these regions or from outside pressure, will cause a considerable increase in the intracranial pressure. It is therefore essential that careful neurologic studies be made to exclude any of the possibilities mentioned before one is justified in suggesting encephalography as a diagnostic measure.

NORMAL ENCEPHALOGRAPHIC OBSERVATIONS

It is not my purpose to discuss the circulation of the cerebrospinal fluid. That has been discussed amply by others—Fremont-Smith and Kubie, Dandy and Blackfan, Frazier and Peet, Kubie, Penfield, Weed and Hughson, Fay and Pancoast and Fay. The theory that the major portion of the cerebrospinal fluid is formed from the choroid plexus is accepted. The interpretation of the roentgenologic observations is also based on the theory that the cerebrospinal fluid passes from the lateral ventricles through the foramens of Monro into the third ventricle, which communicates with the fourth ventricle through the aqueduct of Sylvius. From the fourth ventricle the fluid has three possible means of escape; posteriorly in the midline directly into the cisterna magna through the foramen of Magendie, or by passing laterally and anteriorly around the medulla to reach the anterolateral surface through the foramina of Luschka into the cisterna pontis. The fluid is now in the true subarachnoid space, and from the cisterna pontis it reaches the cisterna chiasmatis. Having reached this point, the fluid may pass in one or all of three directions: (1) the interhemispheric midline over the corpus callosum; (2) the sylvian fissure to the rolandic area, with numerous pathways over the cerebral cortex anterior to this region and few posterior pathways over the occipital lobes, and (3) the cisterna venae magnae cerebri by way of the cisterna interpeduncularis and cisterna intercommunicans. The last pathway is possibly compensatory. Ultimately the fluid reaches the pacchionian bodies or subarachnoid villi at the vertex and over the lateral surfaces of the brain and is eliminated as shown by Weed and his co-workers. In this laboratory it has been assumed that anything which disturbs this circulation will cause structural changes which vary in degree depending on the type of pathologic process and its position. The experimental and clinical observations of Fay and the neuropathologic studies of Winkelman have been invaluable. It was only after careful study and correlation of their observations that I found it possible to make logical roentgenologic deductions, many of which have been confirmed at operation.

In order that one may have a clear conception of the roentgenologic observations that have been adopted as indicative of a normal encephalogram, Dr. Henry K. Pancoast has given permission to publish, in part, the report of the Committee on Standardization of Encephalography. This committee, which consisted of Dr. William C. Spiller, Philadelphia, Dr. Israel Strauss, New York, Dr. Temple Fay, Philadelphia, Dr. N. W. Winkelman, Philadelphia, Prof. W. S. Pardoe, Philadelphia, Dr. Leopold Jaches, New York, myself and Dr. Henry K. Pancoast, Philadelphia, Chairman, was appointed by Dr. Edward H. Skinner of Kansas City, President of the American Roentgen Ray

Society. The committee was to investigate the problems involved in encephalography and to attempt to standardize the operative and roentgenologic technic.

The following is quoted from the report of this committee:

1. Normal encephalographic appearances following the proper operative and roentgenological technic. It was realized that we cannot expect encephalographic procedures to be carried out on normal individuals, and the best that we can do is to declare our judgment as to what is approximately normal from a large number of negative encephalographic studies (figs. 4 and 5).

a. Subarachnoid cortical air markings replacing the usual fluid pathways.

1. Distribution: The Committee agreed that, in the normal these pathways are confined to the frontal and parietal surfaces of the brain over the external

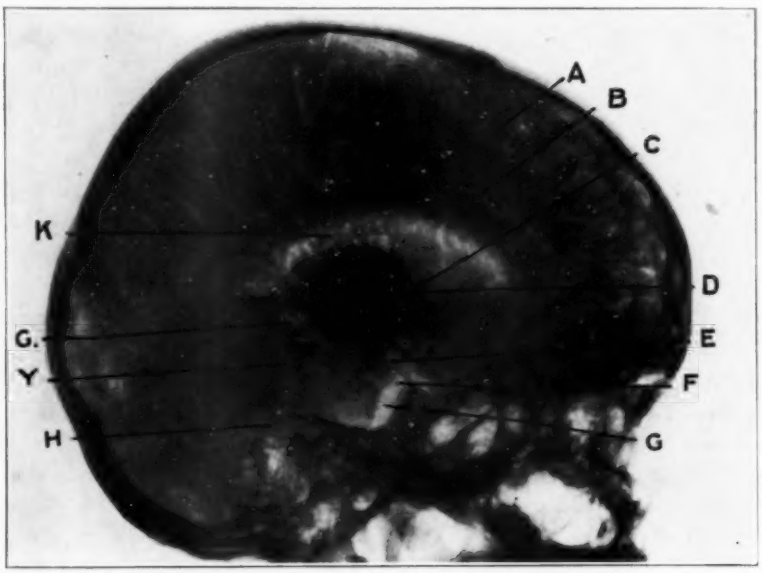

Fig. 4.—Encephalogram, made by Dr. Temple Fay, showing a boy, aged 12, with defective vision (Service of Dr. William G. Spiller). Convulsions began one year before. The diagnosis was epilepsy. Except for a slight increase in the size of the subarachnoid markings in the frontal region, interpreted as beginning atrophy of the frontal lobe, the observations were essentially normal and will be used as descriptive of the normal encephalogram. *A*, normal-sized subarachnoid pathways; *B*, subarachnoid pathway over the corpus callosum; *C*, foramen of Monro connecting the lateral ventricles with the third ventricle; *D*, faintly visible third ventricle, best seen in the stereoscope; *E*, cisterna interpeduncularis; *F*, cisterna chiasmatis; *G*, cisterna pontis; *H*, fourth ventricle faintly visible as a triangle superimposed on the mastoid cells; *I*, aqueduct of Sylvius; *J*, cisternae intercommunicantes which follow the course of the fourth nerves and connect the cisterna venae magnae cerebri with the cisterna interpeduncularis; *K*, lateral ventricles; the descending horns are not visible because they are not filled with air.

cortical surface. The sylvian fissure represents their posterior and inferior boundary, and they are seldom found normally posterior to the parieto-occipital sulcus and a line connecting this point with the sylvian fissure.

Midline: There is a distribution of air, though usually to a much less extent, over the mesial surfaces of the hemispheres above the corpus callosum in the midline, extending from the frontal region to the posterior portion of the paracentral lobule. This can be distinguished from the cortical air by the fact that the lines arise just above the corpus callosum.

The uniform distribution of these markings throughout the frontal and parietal lobes gives a definite cortical pattern in which the brain completely fills its dural casement without signs of fluid spaces existing over the cortex sufficient to give a demonstrable space between the inner table of the skull and the cortex.

The air is within the subarachnoid spaces between the convolutions, following the sulci over the above area of distribution.

2. Size of Markings: These air markings, comparable to hair pin size, vary from 1 to 3 mm. in width on the flat roentgenogram taken at 44 inches' target film distance. The larger width represents the increased size due to projection of pathways from the opposite side of the head. This size also depends upon the roentgenograms being made within one hour after the introduction of air. This time element is a very important item in standardization of technic.

b. Basal Cisternae: If there is sufficient fluid withdrawn and sufficient air injected, the basal cisternae (cisternae magna, pontis, interpeduncularis and chiasmatis) should be plainly visible in the normal. After cisternal puncture, there is usually poor filling of the cisternae pontis, interpeduncularis and chiasmatis, probably because one cannot manipulate the head satisfactorily for adequate distribution when the needle is introduced into the cisterna magna, and there results a water trap effect.

The cisterna magna communicates directly with the upper cervical canal. It is bounded above by the under surface of the vermis, laterally by the cerebellar hemispheres and anteriorly by the medulla. It is continuous with the cisterna pontis through spaces which surround the medulla and pons and is seen only in the lateral views, and should show well normally.

The cisterna pontis surrounds the anterior and lateral surfaces of the pons, and extends anteriorly to the basilar process of the occipital bone. It is seen only in the lateral views, and should show well normally (fig. 4 *G*).

The cisterna interpeduncularis is continuous with the cisterna pontis and is situated anterior to the peduncles of the cerebrum and posterior to the infundibulum. It is triangular in shape in the lateral view, with the apex up and the base continuous with the cisterna pontis. One must be quite familiar with encephalographic relations to make it out (fig. 4 *E*).

The cisterna chiasmatis is seen in the normal as a collection of air situated above the pituitary fossa and extending slightly anterior to it. It is frequently bisected by structures such as the optic chiasm, internal carotid artery and the infundibulum, which then cast perceptible shadows. It is seen on the lateral view only. It varies in size and shape, and the Committee at its first meeting did not attempt to standardize the normal size (fig. 4 *F*).

The cisterna venae magnae cerebri was accepted by the Committee as a normal entity which, they believe, may contain a small amount of air under normal conditions, although any large amounts of air are abnormal. The small collection is situated anatomically above the vermis and extends anteriorly to the quadrigeminal and pineal bodies. It lies just below and anterior to the under surface

of the tentorium in the midline. This cistern is capable of considerable abnormal distention and air will then extend well laterally (fig. 5 *G*).

The cisterna intercommunicans connects the cisterna interpeduncularis with the cisterna venae magnae cerebri. The committee accepts this cistern as an entity. So far they have not found a name for it and have accepted this name until further search can establish some other correct anatomical designation, if any has been given. The cisterna intercommunicans lies bilaterally along the course of the fourth nerve. The air space usually measures 1 to 3 mm. in width upon the roentgenogram. It is seen in the lateral view as two small crescentic lines with the concavity toward the vertex (fig. 4 *J*).

c. The Ventricular System: If the lateral ventricles fill properly, air should be seen also in the third ventricle, aqueduct and fourth ventricle.

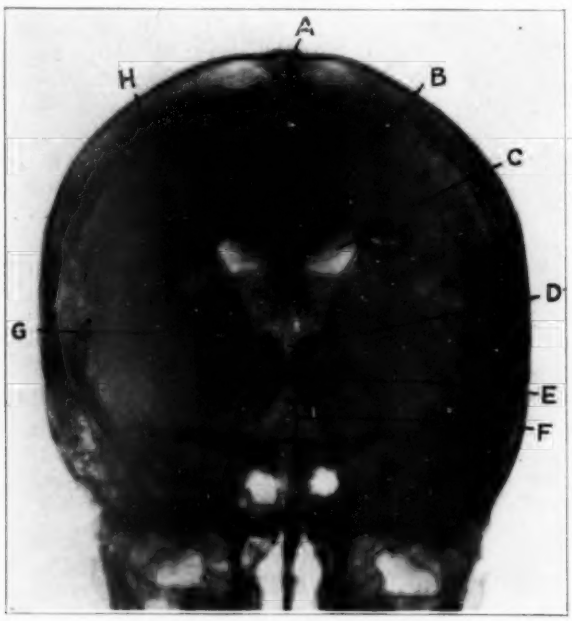

Fig. 5.—Same patient as in figure 4. Anteroposterior position showing normal subarachnoid pathways and normal position of the ventricles. *A*, triangular longitudinal sinus; *B*, subarachnoid air over the corpus callosum; *C*, lateral ventricle; normal appearance when projected on the roentgenogram at the angle; *D*, third ventricle; *E*, aqueduct of Sylvius; *F*, fourth ventricle; *G*, cisterna venae magnae cerebri, and *H*, normal subarachnoid pathways.

The Lateral Ventricles: The exact size and shape of these ventricles cannot yet be established because, up until the present time, there has been no uniformity whatever in the roentgenological technic, and further observations must be made based upon some standardization of the procedure. There must also be a standardization of operative technic.

The Committtee agreed that failure of the ventricles to fill with air should, in the light of our present knowledge, be regarded as the result of an error in operative technic, unless it is satisfactorily proven that a pathological condition

prevents filling. It was further agreed that if the ventricles did not fill, one examination was not sufficient for an assumption that pathology existed. Either another partial examination should be made in twenty-four hours to see if the ventricles were then filled or another complete operative and roentgenological procedure carried out subsequently at a safe period.

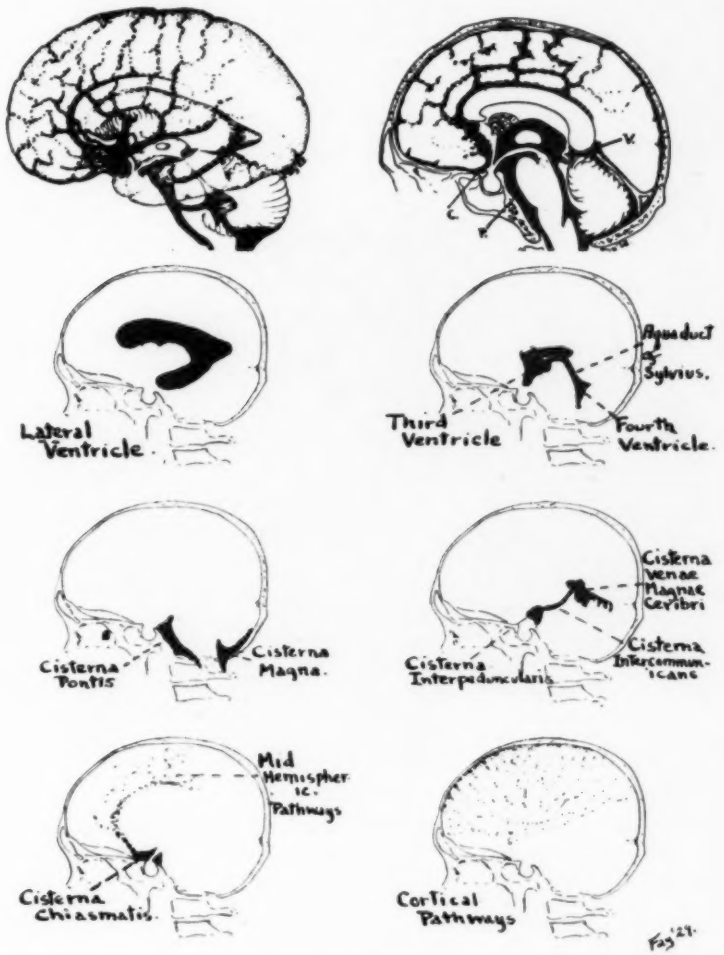

Fig. 6.—Graphic chart showing the fluid spaces of the ventricles, the subarachnoid pathways and the basal cisternae.

It was recognized that obstruction to the passage of air but not to cerebrospinal fluid could exist due to the presence of an arachnoid membrane covering the outlets of the foramina of Magendie and Luschka, such as has been described by Bateman.

With the lateral ventricles properly filled, they should be symmetrical as to size and shape and as to position on each side of the midline. The communication

with the third ventricle through the foramina of Monro should be seen in stereoscopic lateral views (fig. 4 *K*).

Third Ventricle: The outlines of the third ventricle are best seen in stereoscopic lateral views, and also its communication with the fourth ventricle through the aqueduct of Sylvius. The third ventricle should also be seen in the sagittal views, particularly to determine the presence or absence of midline shift. This must depend largely upon proper roentgenological technic (fig. 5 *D*).

The fourth ventricle is clearly seen in the lateral views as a triangle with its apex pointing upward and posteriorly and its base pointing anteriorly and downward. In the anteroposterior roentgenogram it is

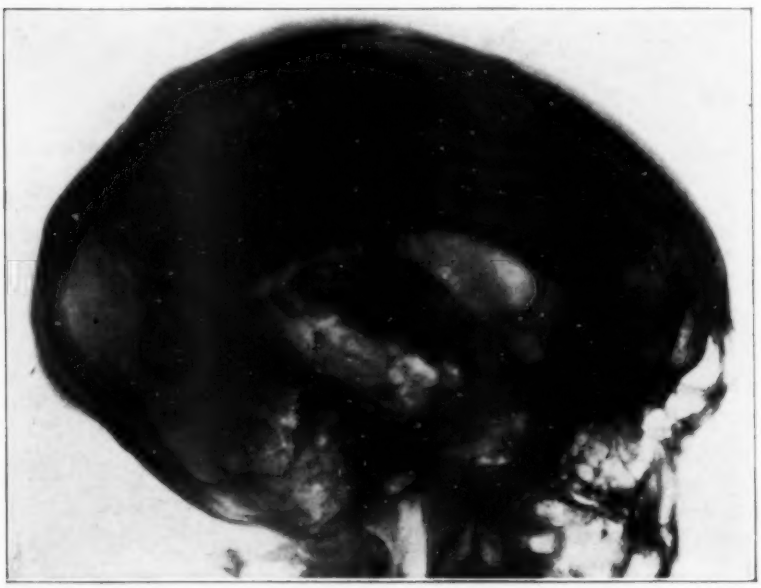

Fig. 7.—Encephalogram, made by Dr. R. B. Bromer, showing normal subarachnoid pathways, basal cisternae and ventricles in a man, aged 25 (service of Dr. Temple Fay, Episcopal Hospital). The unusual feature is the complete drainage of the descending horns of the ventricle and replacement with air. This was possible after extreme manipulation of the head.

clearly seen as a midline triangle with base down and apex upward (figs. 5 *F* and 6).

The lateral ventricles are not usually seen in their entirety, because of lack of drainage of the posterior and inferior horns. In some cases by extreme manipulation it is possible to drain these areas (fig. 7), but I have found that when it is advisable to demonstrate the entire ventricles, the patient can be taken in the positions used in ventriculography (Pendergrass, 1927), which require the patient to lie in the horizontal lateral position, the Coolidge tube being below the table and the film

above the patient. This allows the fluid in the upper ventricles to drain into the dependent ventricle and the former to fill with air which is then projected on the film.

ROENTGENOGRAPHIC APPEARANCES IN VARIOUS PATHOLOGIC CONDITIONS

The following pathologic conditions can be demonstrated on the roentgenogram after encephalography:

1. Atrophy of the brain
   (*a*) Of external hydrocephalus
   (*b*) Of internal hydrocephalus
   (*c*) Combination of internal and external hydrocephalus.
   (*d*) Following thrombosis
2. Aplasia
3. Arachnoiditis
4. Porencephaly
5. Tumors of the brain or mass lesions

Atrophy of the Brain in External Hydrocephalus.—An interpretation of atrophy of the brain is made from the encephalogram in cases that show: (1) an increase in the size of the subarachnoid cortical markings; (2) an increase in the size of the basal cisternae, especially the cisterna venae magnae cerebri, and (3) the presence of subarachnoid air over the occipital and temporal lobes. As already stated, I have accepted as fact the observations of Weed, which are mainly that normally the major portion of the subarachnoid fluid circulation is eliminated over the frontal and parietal regions, especially by the subarachnoid villi and pacchionian bodies situated adjacent to the longitudinal areas. Dandy pointed out that, grossly, cerebrospinal fluid is found rarely over the temporal or occipital lobes or the under surface of the frontal lobes in the normal person. If these premises are true, then the presence of subarachnoid markings over the occipital and temporal lobes may be regarded as compensatory pathways.

The degree of atrophy is subdivided into stages: slight, moderate and advanced. Having assumed an arbitrary scale for the normal subarachnoid space as being from 1 to 3 mm. in width, I regard anything over this size as evidence of slight atrophy. The question was raised in some cases that were diagnosed as slight atrophy of the brain whether or not a temporary dilatation of subarachnoid pathways was present at the time of the examination. I believe that temporary dilatations of the subarachnoid spaces do exist at times, but I think that drainage of the spinal fluid probably would remove the cause of temporary dilatation. Another question was whether the replacement of the fluid with air did not at times increase the size of the subarachnoid spaces. I do not

think that this is probable when the technic is performed as recommended; that is, when the spinal fluid has been replaced with air by the pressure per pressure method instead of by the volume per volume method.

Moderate atrophy of the brain is interpreted from encephalograms showing marked increase in the size of the subarachnoid spaces, with small collections of air at the vertex and an increase in the size of the basal cisternae, especially the cisternae venae magnae cerebri, and finally a few compensatory pathways over the occipital lobes (fig. 8).

Advanced atrophy is the interpretation when the encephalogram shows large collections of air over the two hemispheres of the brain, with

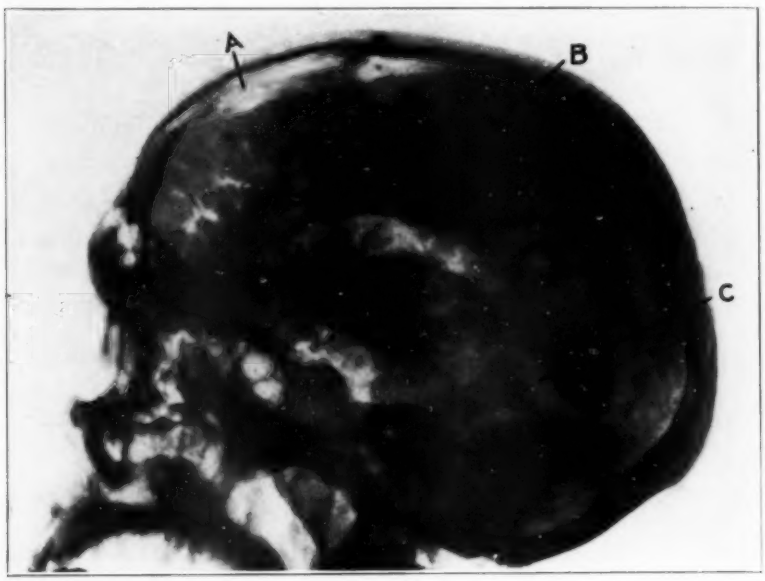

Fig. 8.—Encephalogram of a man, aged 38, with a diagnosis of posttraumatic necrosis and a history of a severe accident six months before, with concussion of the brain and bleeding from the ears (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. James Gardner. There is a marked increase in the size of the subarachnoid markings in the frontal region, with a large collection of air at the vertex (*A*). There is an absence of markings in the parietal region (*B*). These observations were interpreted as atrophy of the brain in the frontal region with arachnoiditis in the parietal lobes. Note the difference between these appearances and those in the so-called normal brain in figures 4 and 5. There is no deformation of the ventricles. The atrophy is of the superficial type. Note the large compensatory pathway at *C*, the cisterna venae magnae cerebri.

air in the midline in the region of the falx showing some separation of the mesial surfaces, increase in the number of compensatory pathways and enlargement of the basal cisternae (fig. 9). In all these cases, there

is a marked increase in the amount of cerebrospinal fluid that is drained at the time of replacement with air.

Atrophy of the Brain in Internal Hydrocephalus.—I was able to demonstrate two types of internal hydrocephalus: (1) In cases in which some anomaly or pathologic condition was present in the region of the foramina of Luschka and Magendie, long-standing enough to cause an internal hydrocephalus and subsequent atrophy of the brain, the circulation became reestablished following some unknown factor, and at the time of the examination no increased intracranial pressure was evident. In these cases, the encephalogram demonstrated a uniform dilatation of all of the ventricles without any particular change in the subarachnoid markings. (2) In one case I was able to demonstrate a unilateral

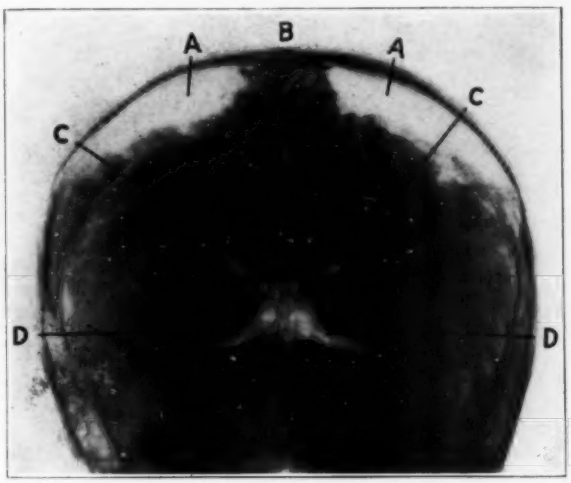

Fig 9.—Encephalogram of a man, aged 30, with a history of mental deterioration (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. James Gardner. Note the marked bilateral cortical atrophy at *A*, indicated by the space between the brain and the vault. The longitudinal sinus can be seen at *B* with adjacent brain tissue on each side. The lateral ventricles can be seen at *C*. There is no deformation. The cisterna venae magnae cerebri is considerably enlarged forming a tent shadow, corresponding to the under surface of the tentorium (*D*); 245 cc. of spinal fluid was drained from this patient.

dilatation of one lateral ventricle (figs. 10 and 11). I assumed that the affected ventricles had a block at the foramen of Monro on one side long enough to cause extreme dilatation of the affected ventricle with subsequent brain atrophy. The reestablishment of the circulation was evidenced by the ability to drain and fill this dilated ventricle by the lumbar route. A cortical lesion could not explain such a uniform dilatation of the ventricle.

Atrophy of the Brain Combined with External and Internal Hydrocephalus.—If the pacchionian bodies and subarachnoid villi eliminate the major portion of the cerebrospinal fluid, anything that disturbs the elimination of the cerebrospinal fluid ultimately will tend to cause external and internal hydrocephalus. My encephalographic interpretations can be explained only by the factors of hydraulics pointed out by Weed, Fay and Winkelman. The subarachnoid pathways or fluid spaces are the first to suffer behind the point of obstruction. They dilate, and the back pressure is next transmitted to the basal cisternae, and then finally to the fourth, third and lateral ventricles, the last being least affected according to these authors. The encephalographic observations in such cases are: collections of air at the vertex, an increase in the

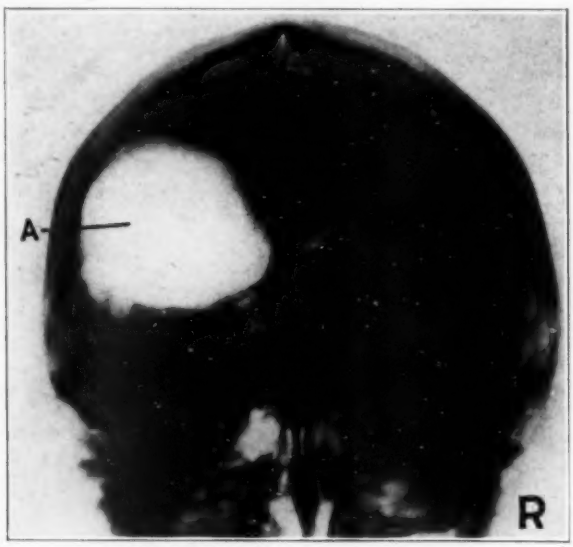

Fig. 10.—Encephalogram of a boy, aged 14, with a history of jacksonian epilepsy with difficulty in speech (service of Dr. Charles H. Frazier, University Hospital). There was very little movement of the right arm and leg and a decided limp on walking. The encephalogram was made by Dr. James Gardner. Note the large dilatation of the left ventricle with almost complete disappearance of the brain cortex on the affected side. The midline structures have shifted toward the affected side, indicating an absence of increased pressure on the left. The fact that the ventricles are filled with air indicates that the foramen of Monro is patulous. There are two possible explanations of the abnormality: (*a*) temporary obstruction of the foramen of Monro of the left ventricle, long-standing enough to cause the dilatation and atrophy of the brain, which at some subsequent time had its normal circulation reestablished with subsequent retraction of the unaffected side toward the affected one; or (*b*) a large porencephaly of the left side which involved the entire lateral ventricle.

subarachnoid markings, compensatory subarachnoid markings, increase in size of the basal cisternae and slight dilatation of the ventricles, the lateral ventricles suffering least (figs. 12 and 13).

There is another type of lesion that causes unilateral internal hydrocephalus and either unilateral or bilateral external hydrocephalus. Following trauma, some cases show a subcortical lesion, which in healing and subsequent contraction of the scar causes unilateral dilatation of the ventricle on the affected side and unilateral retraction of the surface of the brain toward the lesion (fig. 14). If there has been enough

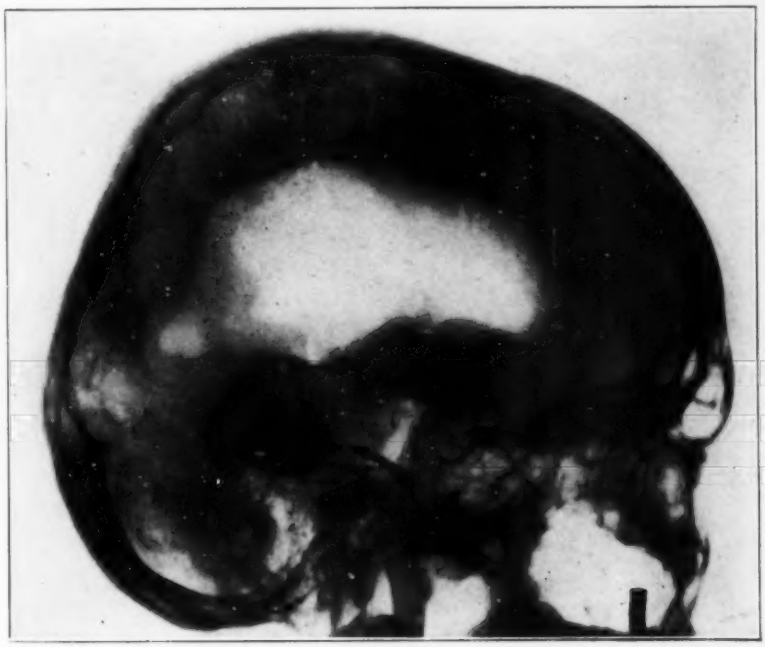

Fig. 11.—Lateral view of the same patient as in figure 10. Note the large uniform dilatation of the lateral ventricle. It is clear why this patient had motor disturbances and speech defects owing to marked atrophy involving these portions of the brain. The subarachnoid markings on the opposite side are within normal limits.

free bleeding to cause generalized obstruction at the points of elimination, the external hydrocephalus may be bilateral.

The encephalographic observations in such a case would be as follows: a unilateral dilatation of the ventricle with elevation of its roof, possible displacement of the midline structures toward the affected side, a unilateral collection of air over the cortex due to retraction of the brain cortex and an increase in size of the subarachnoid markings elsewhere.

The most confusing type of atrophy of the brain occurs in cases in which there is an associated arachnitis which causes laking of the cerebrospinal fluid in the subarachnoid spaces as described by Dandy. As Fay has explained, it is impossible to manipulate the head in such a way as to cause a drainage of these areas, because of an obliteration or narrowing of the normal pathways. If the fluid is not drained, of course, no air can replace it. Fay compares the phenomenon to that of a "narrow neck bottle" which requires the actual shaking out of fluid to permit its replacement by air. Other areas may be sponge-like and trap the fluid within the meshes of reactive tissue. Atrophy is present, indicated

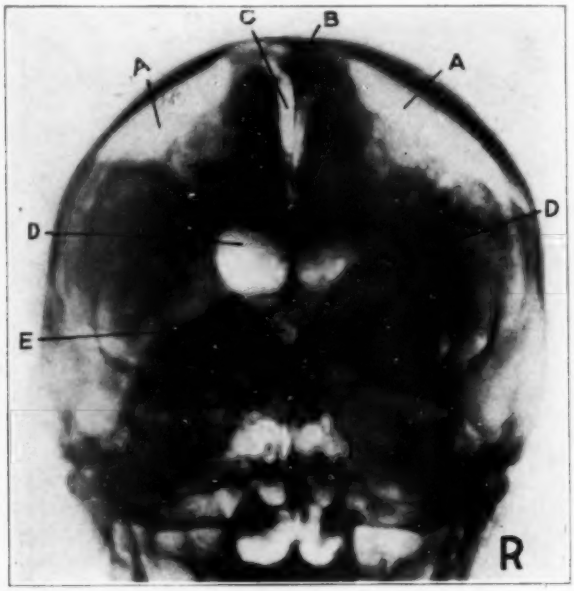

Fig. 12.—Encephalogram of a man, aged 60, who had progressive right hemiparesis with motor aphasia (service of Dr. William G. Spiller). The encephalogram was made by Dr. Temple Fay. The anteroposterior view shows marked bilateral atrophy indicated by the large subarachnoid spaces at *A*. The longitudinal sinus is seen at *B*. There is a large collection of air in the interhemispheric spaces at *C*. The lateral ventricles seem larger than normal, and the left is larger than the right (*D*). The explanation for the increased size of the left ventricle may be explained by a subcortical lesion, which may have been caused by a thrombosis of one of the large arteries. This would also explain the right hemiparesis. The third ventricle can be seen at *E*.

by dilatation of the ventricles and by an increase in the amount of the cerebrospinal fluid drained from the canal.

The encephalogram in such a case may show an absence of cortical subarachnoid air markings which may make one think of arachnoiditis,

yet disguise an underlying atrophy of the brain because of undrained fluid, and differentiation from plastic arachnoiditis should be borne in mind (fig. 15). The ventricles are usually dilated, as are the basal cisternae.

Atrophy of the Brain Following Thrombosis.—Atrophy occurring in thrombosis follows the vascular plan of distribution and is different from the atrophy found in cases of external hydrocephalus, which follows the plan of the subarachnoid distribution of the cerebrospinal fluid. The encephalographic observations in such a case are those of a unilateral cortical atrophy which causes a unilateral internal and external

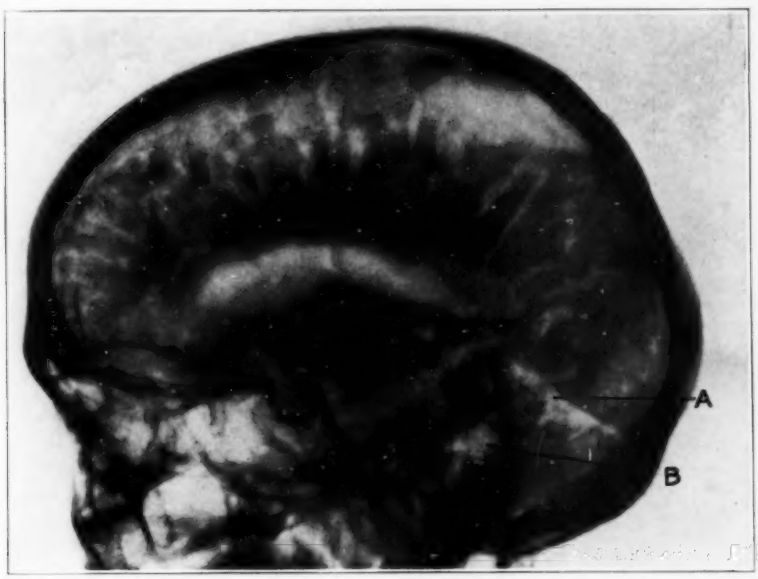

Fig. 13.—The same patient as in figure 12. Note that the position of the atrophy is largely limited to the frontal and parietal areas. This was a constant observation. The enlarged cisterna venae magnae cerebri can be seen at *A*. The fourth ventricle is enlarged (*B*). It is triangular, the apex being posterior and the base anterior. In this case 255 cc. of fluid was removed. Compare these appearances with those seen in figures 8 and 9.

hydrocephalus. The degenerative process causes a shrinkage of the cortical tissue which retracts the walls of the ventricle on the affected side and surface of the brain toward the lesion. If the thrombus occludes a large vessel, the midline structures may be displaced toward the affected side for the same reason, namely, the contracture of the scar (figs. 15 and 16).

The report of the encephalographic committee on atrophy of the brain is quoted in its entirety because of the importance of this subject.

a. It was accepted by the committee that the generalized shrinkage and atrophy occurring in the frontal and parietal areas is a pressure atrophy of the ischemic type. This was based largely but not entirely upon the conclusive results of the investigations of Dr. Winkelman upon atrophic areas of brain tissue in cases of alcoholism, paresis and epilepsy, and compared with non-atrophic areas, and in which he found the atrophy due directly to decrease in blood supply from pressure and not primary vascular changes. Changes produced by pressure atrophy are confined for the most part to the ganglion cells of the cortex and secondarily to the white matter. It was accepted at this time that the major evidences were

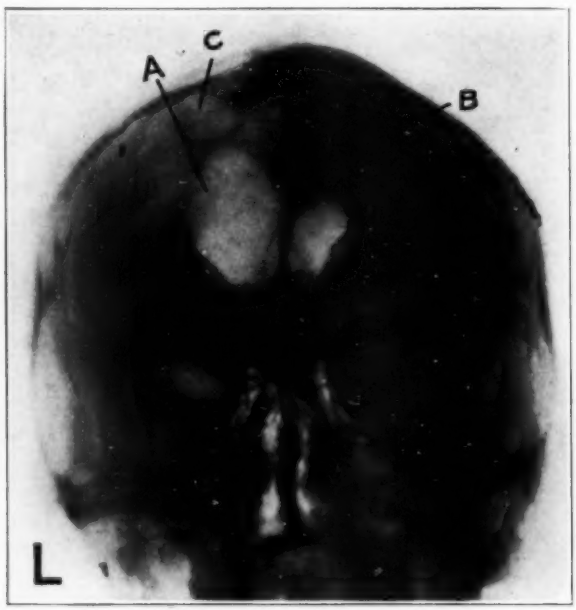

Fig. 14.—Encephalogram of a girl, aged 17, in whose case a diagnosis of posttraumatic epilepsy was made (service of Dr. C. H. Frazier, University Hospital). The encephalogram was made by Dr. James Gardner. In the anteroposterior view, one can see the unilateral dilatation of the left ventricle in the region of the fractured skull which was operated on. The rarefied area at *C* is not a collection of subarachnoid air but is due to the absence of bone, removed at the time of the previous operation. Note the absence of subarachnoid pathways at *B*. These observations were interpreted as subcortical brain atrophy on the left, deforming the left ventricle, and bilateral plastic arachnoiditis indicated by the absence of subarachnoid pathways; 115 cc. of fluid was drained from this patient.

in favor of the elimination of the fluid through the subarachnoid villi and the pacchionian bodies, although this subject was to come later for detailed discussion. On this basis, the pressure mechanism consists of a delay in the escape of the cerebrospinal fluid from the channels over the frontoparietal area, thereby permitting excessive accumulations in the subarachnoid space.

The factors underlying these disturbances are probably those which impair or destroy the function of the pacchionian bodies or subarachnoid villi, such as free hemorrhage in the subarachnoid space, trauma including birth injury, inflammatory or toxic processes and infiltrative processes such as metastatic carcinoma.

The fluid accumulations would respond to the laws of hydraulics, so that within the rigid confines of the skull a pulsating distribution of pressure would act directly on the walls of the fluid channels. Changes of pressure are produced by overproduction of fluid compared to its escape, by coughing, straining, crying and other exertions. They temporarily or more or less permanently cut down the capillary vascular supply, and with a fixed fluid "cast," favor pressure atrophy through ischemia, or favor lack of normal development.

b. The escape of the under surface of the frontal lobes and the temporal and occipital lobes from this type of atrophy cannot be explained upon the basis of a disturbed vascular plan, but it does conform with the area of cortical cerebro-

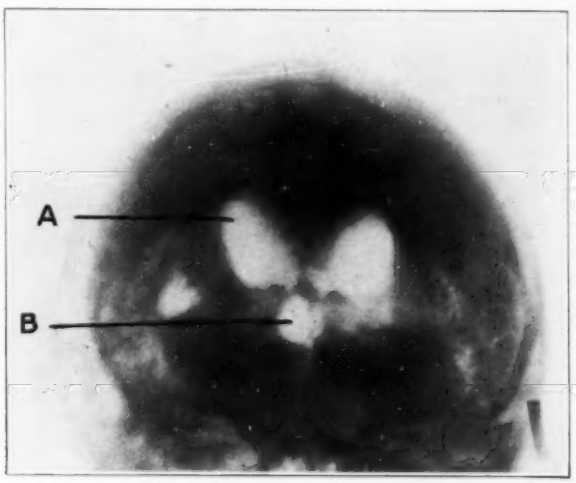

Fig. 15.—Encephalogram of a man, aged 56, with a history of left sided hemiplegia and visual disturbances (service of Dr. William G. Spiller). The encephalogram was made by Dr. James Gardner. It indicates slight subcortical brain atrophy on the right side, causing some deformation and slight elevation of the roof of the right ventricle seen at *A*. The third ventricle at *B* and the midline structures are displaced to the right, probably owing to subcortical atrophy on the affected side. The absence of subarachnoid markings may be due to arachnoiditis, but I felt that there was an underlying disguised atrophy of the brain, which was impossible to demonstrate owing to the absence of drainage of the fluid which may have been trapped.

spinal fluid circulation. For this reason the atrophy usually seen involves the frontal and parietal cortical areas, and especially in the opercular region. Occasionally the cerebellum and the first and second temporal convolutions are involved. Pressure atrophy has been found to occur in the temporo-occipital area only in those cases in which cerebrospinal fluid pathways have been diverted due to an obstruction in the anterior circulating field.

c. It was accepted by the committee that this type of pressure atrophy was easily distinguishable pathologically and roentgenologically from areas of softening due to vascular lesions.

d. Distribution of atrophy confined to one of the cerebral arterial branches, in the presence of a definite history of a vascular lesion, will be interpreted as such when collections of air are found corresponding to the vascular plan, whereas generalized increased amounts of subarachnoid cortical air represent pressure atrophy.

Increased amounts of air seen over the cortex in encephalograms may be ascribed to two processes:

1. Those produced by pressure atrophy.

2. Those produced by a lesion within the substance of brain causing an area of degeneration as secondary to thrombosis, followed by a fibrosis and gliosis, with contraction, drawing the cortex and ventricular surfaces more closely

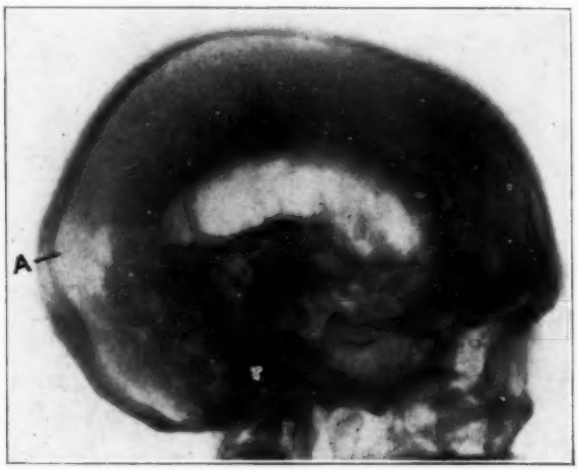

Fig. 16.—The same patient as in figure 15. There are very few subarachnoid markings except over the temporal lobes; these are difficult to demonstrate in the print. The lateral ventricles seem larger than normal. There is a large collection of subarachnoid air over the occipital lobes in the region of the cuneus, seen at *A*. This increased air was interpreted as atrophy, and it was thought that atrophy in the region of the cuneus explained the disturbances in vision.

together. The appearance will be that of an enlarged ventricle with little or no midline shift and an area of increased air over the cortex on the same side. A failure of air to appear over the cortex in this manner may be considered as being due to an inability of fluid to properly drain out because of some obstructive process or to an obliterative plastic arachnoiditis and consequently loss of subarachnoid cortical air markings.

APLASIA

In at least one case in which I made the diagnosis of atrophy of the brain it was the belief of the attending neurologist that the case was not one of atrophy, but of aplasia (figs. 17 and 18). The encephalographic

observations cannot be differentiated from those in external hydrocephalus. This condition is mentioned because of the inability to distinguish between the two conditions; if one is to distinguish between them it will have to be along clinical lines, or possibly the differentiation can be made only by the pathologist, and this would be exceedingly difficult. The significant fact is that aplasia is a clinical and pathologic entity, and this should be borne in mind by the roentgenologist and neurologist. In cases in which there is a history of deficient development from birth or even from early childhood, it would seem more scientific if the

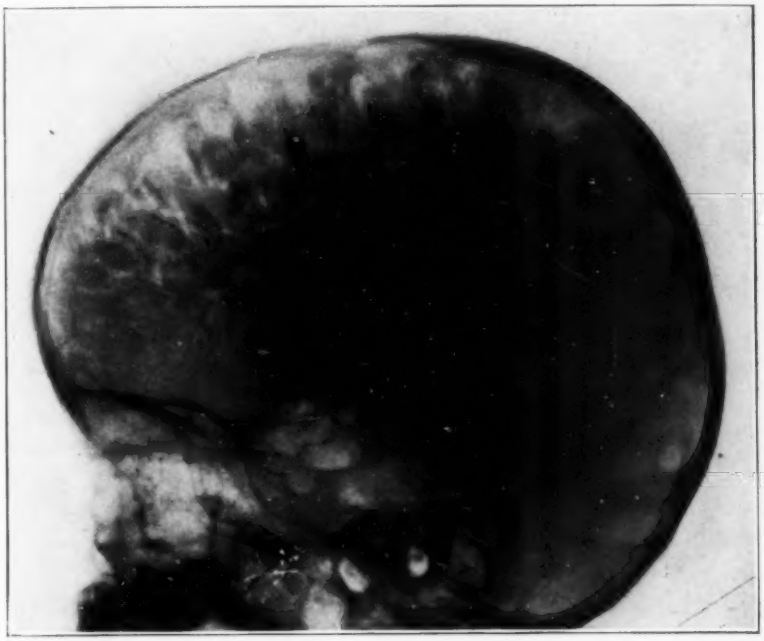

Fig. 17.—The same patient as in figure 16. The lateral view shows that the distribution of the enlarged subarachnoid pathways is limited to the frontal and parietal areas and in the region of the insula of Reil. The basal cisternae are enlarged. In other patients whose condition was diagnosed as idiocy the same peculiar type of enlargement of the subarachnoid pathways was found. The appearance is so unusual that the possibility of idiocy was suggested by the encephalographic observations alone, without any aid from the history. These observations may be indicative of aplasia instead of atrophy of the brain.

roentgenologist would qualify the report on such a case as presenting encephalographic appearances that may be regarded as evidence of aplasia or possibly of atrophy of the brain. Then the neurologist with the clinical facts at hand would be able to give a presumptive diagnosis.

ARACHNOIDITIS

In arachnoiditis, the encephalogram may show a complete absence of the subarachnoid pathways, or it may show a unilateral absence or only a small localized area in which the subarachnoid cortical pathways are not seen. In such cases stereoscopic roentgenograms are invaluable, as it is possible to have subarachnoid pathways of both sides of the cortex projected on a single roentgenogram. With stereoscopic views one can differentiate between the sides of the brain and see them as if the brain were being held in the hand. In marked cases of arachnoiditis, there seems to be a slight internal hydrocephalus which may be due to back pressure (fig. 19).

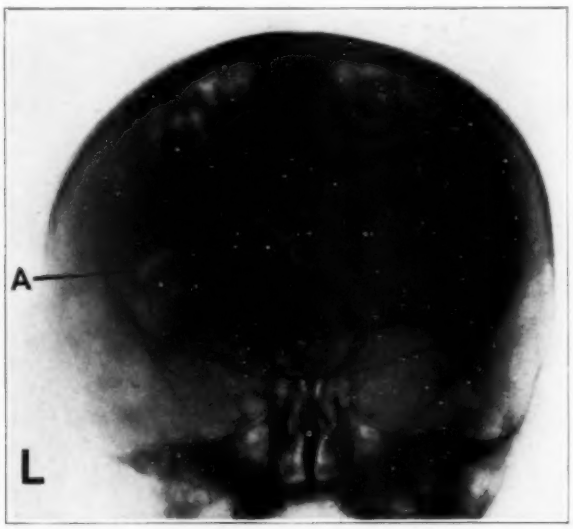

Fig. 18.—Encephalogram of a girl, aged 3, in whom the diagnosis was idiocy (service of Dr. Charles H. Frazier, University Hospital). Labor had been difficult. The child never talked, and walking was delayed; progressive dementia was present. The encephalogram was made by Dr. James Gardner. Increased subarachnoid pathways were shown in the frontal and parietal regions, which was interpreted as atrophy of the brain. The right lateral ventricle was not filled. This was thought to be due to an error in technic. Note the atrophy in the region of the insula of Reil. This may explain the disturbance in speech.

It should be borne in mind that the absence of subarachnoid cortical markings does not always indicate an uncomplicated case of arachnoiditis. The arachnoiditis may be associated with marked, moderate or slight atrophy of the brain in which it is not possible to drain the trapped fluid and replace it with air. When the history suggests such a possibility or when evidences appear in other areas on the roentgenogram, the roentgenologist should make a qualified report.

PORENCEPHALY

Porencephaly, according to Jaffé (1929), usually is defined as a funnel-shaped defect of the brain which extends from the surface of a hemisphere close to or into the lateral ventricles. The defect is covered by a membrane of varying thickness and is filled with a clear colorless fluid; thus, on external examination it appears like a cyst. Although the lesion is supposed to be rare, I have seen two cases within the past year. I believe that with the increased use of encephalography this lesion will be found less infrequently. In an excellent article, Jaffé (1929), reviewed the literature on porencephaly. The preponderance of the

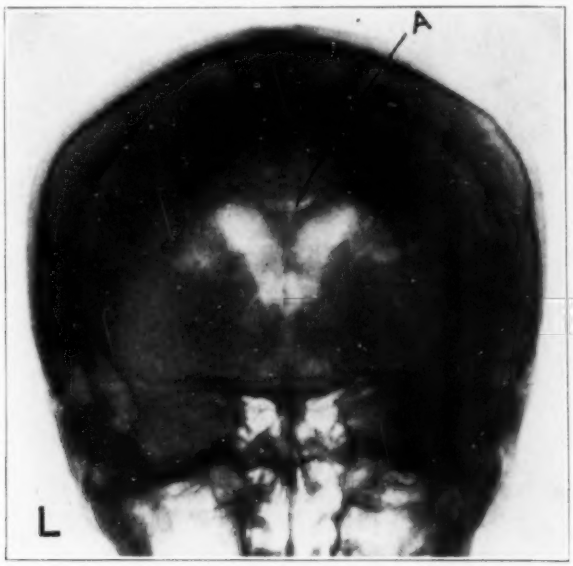

Fig. 19.—Encephalogram of a youth, aged 20, with right-sided paralysis and motor aphasia (service of Dr. Charles H. Frazier, University Hospital). The anteroposterior view shows a complete absence of subarachnoid markings on the left side, which was interpreted as plastic arachnoiditis. This was confirmed at operation. The subarachnoid markings are normal on the right. The subarachnoid air can be seen over the corpus callosum at *A*. The ventricles, all of which can be seen, are normal.

evidence emphasizes the importance of trauma as the etiologic factor in the causation of this interesting pathologic phenomenon. The trauma may occur before birth, at the time of birth or afterward. He also quoted authors who believe that the lesion is a congenital defect. He described the microscopic observations at length and stated that the lesions occur in certain places in the following order of frequency: central convolutions, insula of Reil, parietal region and finally occipital lobe, which was found affected in 14 per cent of the cases.

In one of the cases the lesion occurred in the occipital region and the other in the parietal region. The encephalographic observations in porencephaly are rather typical when the lesion communicates with the ventricle (figs. 20, 21 and 22). The porencephaly communicated with the posterior horn in my two cases. The lesion was circular and contained a fluid level because it was most difficult to drain entirely by the lumbar route. Not infrequently, porencephaly will cause bone atrophy, which may be ascribed to the transmission of a constant pulsation to the adjacent bone.

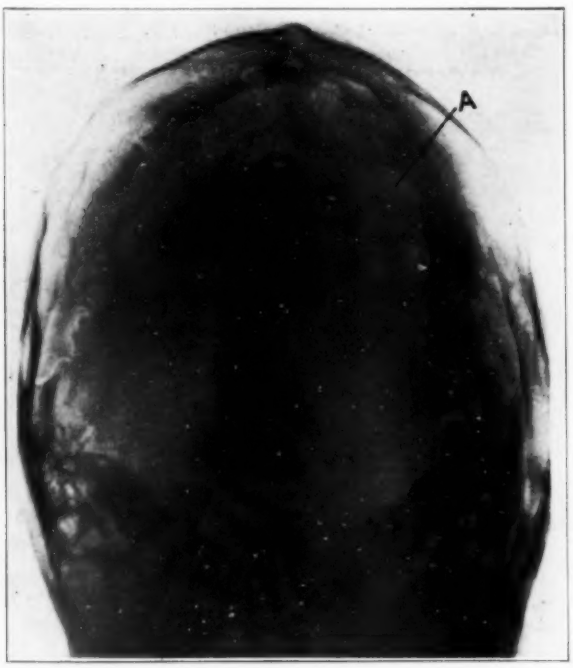

Fig. 20.—Encephalogram of a youth, aged 19, in whom the diagnosis of epilepsy had been made (service of Dr. Charles H. Frazier, University Hospital). The anteroposterior view shows a large irregular area of bone atrophy in the right occipital region. Compare with the opposite side. This examination was made before the encephalography was used.

TUMORS OF THE BRAIN AND MASS LESIONS

Encephalography has been of value in diagnosing tumors and mass lesions of the brain, when the symptoms were vague and not of value for localization. The procedure was utilized only in cases in which there was no increase or only a slight increase in the intracranial pressure. The encephalographic observations depend entirely on the location of the tumor. The tumor may cause a displacement of the midline structures or a deformation of the lateral ventricles or both (figs. 23, 24, 25 and

26). Another observation that has been particularly noticeable is the bilateral absence of subarachnoid pathways. This is difficult to explain. Some of my confrères have felt that the presence of a tumor will cause an "ironing out" of the subarachnoid spaces due to an infiltrative lesion or the flattening of the convolution and an obliteration of the sulci and fluid pathways by pressure from the increase volume of the tumor mass.

ERRORS IN TECHNIC

Several points should be stressed with regard to the interpretation of encephalograms which may be considered under the heading of errors in technic.

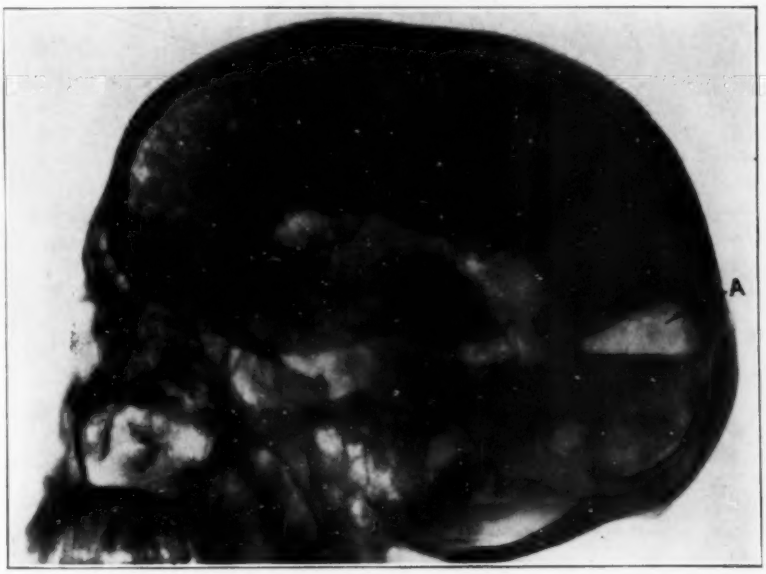

Fig. 21.—The same patient as in figure 20 after an encephalogram had been made. The lateral view shows a typical porencephaly at *A* which communicates with the posterior horn of the lateral ventricle. Note the fluid level with air above it. There is a slight increase in the subarachnoid markings in the frontal region. The porencephaly lies adjacent to the area of bone atrophy seen in figure 20.

Occasionally, in the encephalogram one will find a complete absence of filling of the ventricles with air (figs. 27, 28 and 29). This usually means that the surgical technic of drainage of the cerebrospinal fluid and replacement with air has not been adequate, and therefore should be regarded as an error in technic unless one has strong clinical evidence to the contrary. I have noticed that the absence of filling of the ventricles is almost proportional to the experience of the operator. The inexperi-

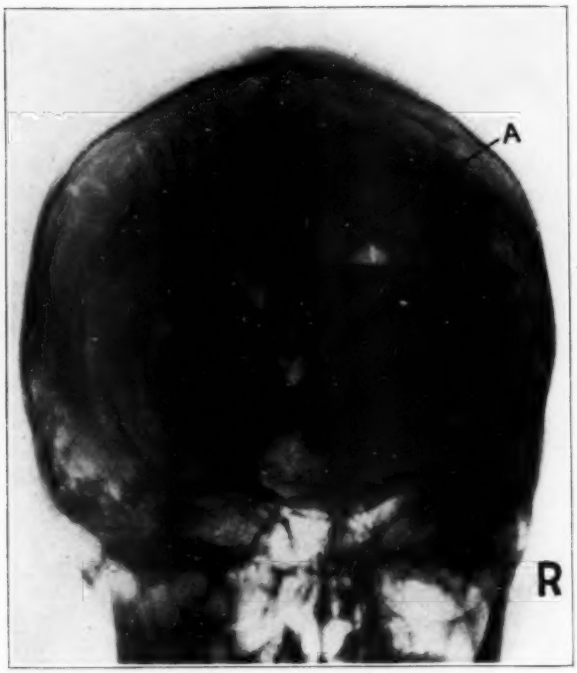

Fig. 22.—The same patient as in figures 20 and 21. The anteroposterior view demonstrates the porencephaly which is in close relationship with the area of bone atrophy. The air and fluid level can be seen.

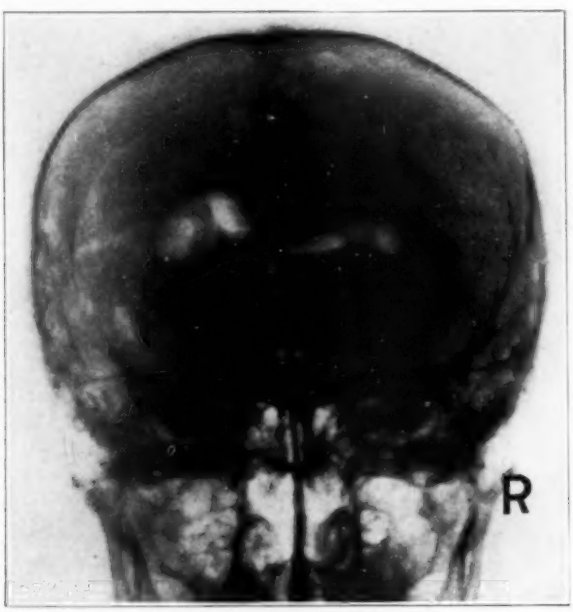

Fig. 23.—Encephalogram of a woman, aged 47, who had jacksonian epilepsy, with weakness of the left arm and leg (service of Dr. William G. Spiller, University Hospital). The encephalogram was made by Dr. F. C. Grant. Note the depression of the roof of the right lateral ventricles. The midline structures are slightly displaced to the left. Note the absence of the subarachnoid pathways.

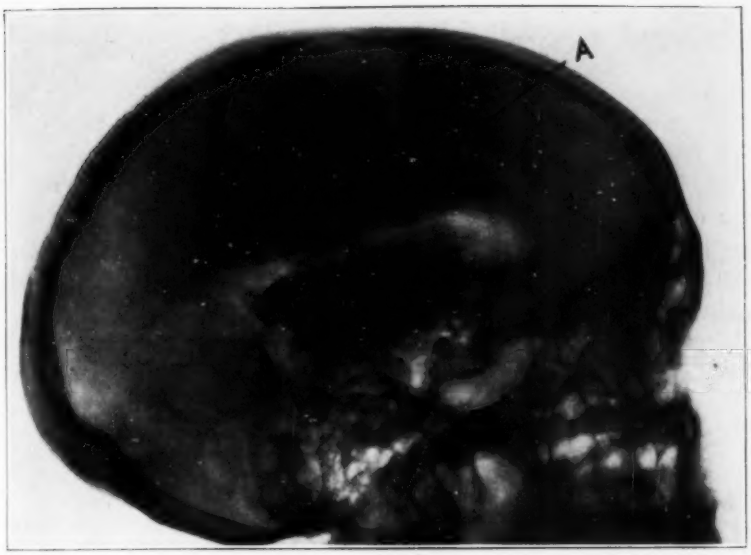

Fig. 24.—The same patient as in figure 23. The lateral view shows a depression of the roof of the lateral ventricle at *A*. The single print is rather confusing as the normal ventricle is superimposed on the affected ventricle. A diagnosis of tumor of the brain was made. At operation an endothelioma of the falx was removed.

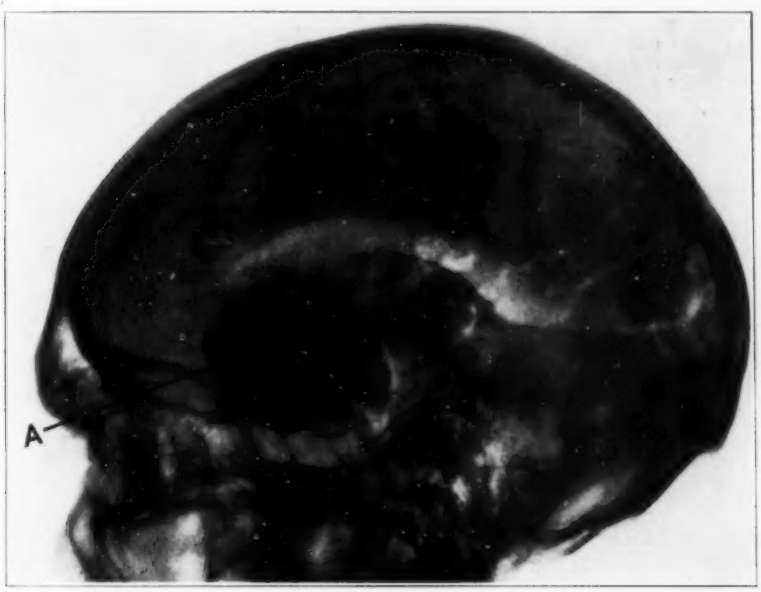

Fig. 25.—Encephalogram of a blind man, aged 50, who had a large suprasellar tumor (*A*), probably a cyst of Rathke's pouch (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. F. C. Grant. The lateral view of the encephalogram shows a complete absence of subarachnoid pathways in the frontal region possibly due to an obstruction of the cisterna chiasmatis. There are compensatory pathways in the occipital region. The ventricles are not obstructed even though the tumor is large.

enced operator is satisfied with much less manipulation of the head than the experienced operator. If a roentgenogram is made twenty-four hours later the ventricles may contain air, which would exclude a pathologic lesion occluding the foramina of Luschka and Magendie. Some of my confrères have stated that they believed the absence of filling in such cases was due to a collapse of the cortex into the ventricles which prevented their filling. I believe that I have proved that this is not the case, because in advanced cortical atrophy of external hydrocephalus there is no deformation of the ventricles (fig. 9). Another

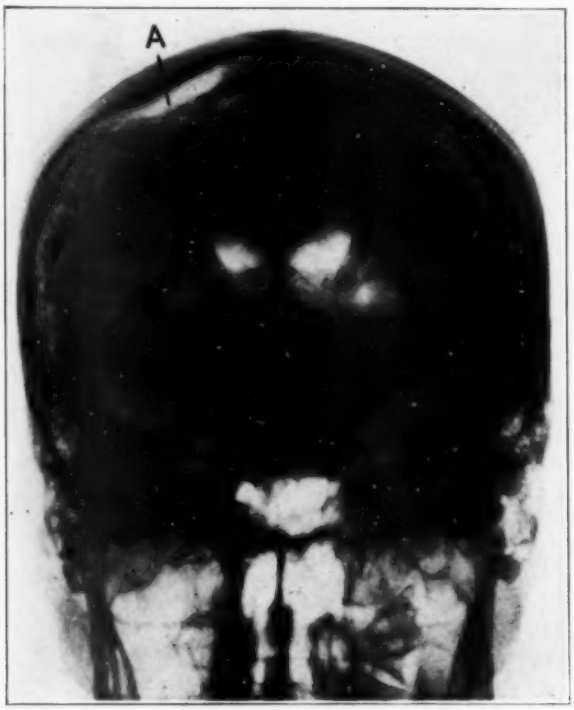

Fig. 26.—The same patient as shown in figure 25. The anteroposterior view does not show any deformation or deviation of the ventricles. There is marked atrophy of the right parietal cortex (*A*). This suggested no explanation unless that there was some obstruction at the outlets.

explanation may be that suggested by Bateman (1928), who said that he had demonstrated a membrane that is not permeable to air. If this type of membrane covered the foramina of Luschka or Magendie, the absence of the filling of the ventricles could be explained. There are still other physiologists who do not believe that there are normal openings or foramina such as described by Luschka and Magendie, and that when found they are produced by trauma. The explanation of filling

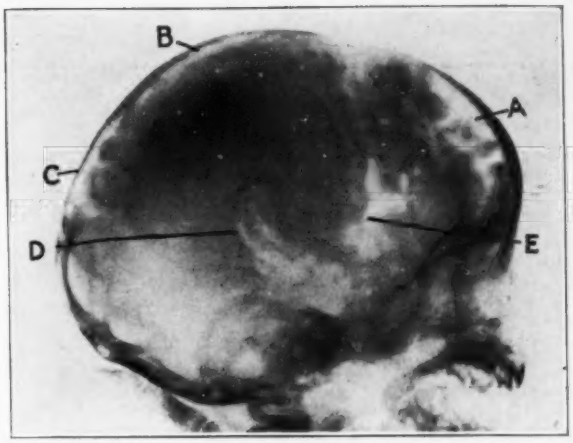

Fig. 27.—Encephalogram of a female infant, aged 8 months, in whom the clinical diagnosis was splastic paraplegia with cerebral and optic atrophy (service of Dr. Charles Cole). The encephalogram was made by Dr. Temple Fay and Dr. Shumaker. There had been a difficult forceps delivery. The infant had convulsions on the third day; these were present intermittently for four days. The encephalogram shows an absence of filling of the lateral ventricles owing to insufficient drainage. There is evidence of marked atrophy in the frontal region at *A*, in the region of the island of Reil at *E* and in the parietal and occipital lobes at *B* and *C* which would probably account for all of the patient's symptoms. Enlargement of the cisternae intercommunicans is clearly visible at *D*.

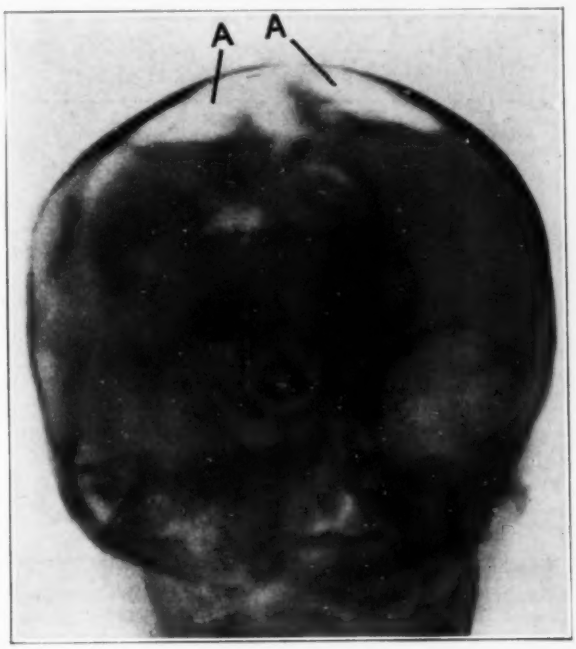

Fig. 28.—Encephalogram of a female infant, aged 9 months, with spastic diplegia; the diagnosis was Little's disease (service of Dr. Charles Fife, Mary Drexel Hospital). The encephalogram was made by Dr. Fay and Dr. Shumaker. There was a history of birth trauma. The anteroposterior view shows evidence of bilateral cortical atrophy at *A*. Possibly this should be regarded as an aplasia instead of atrophy.

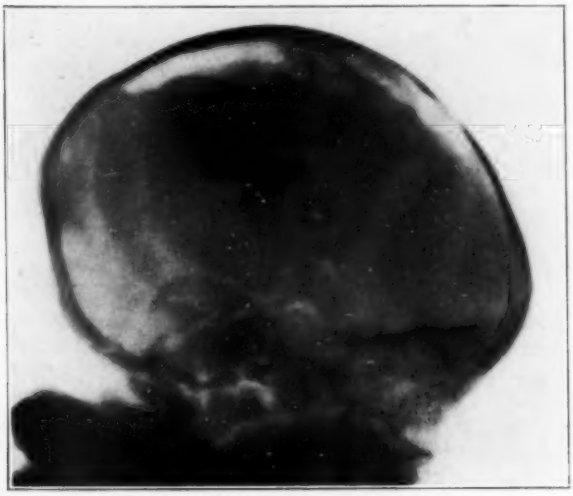

Fig. 29.—The same patient as in figure 28. The ventricles are not filled. The increase in the subarachnoid spaces is distributed in the frontoparietal and occipital regions.

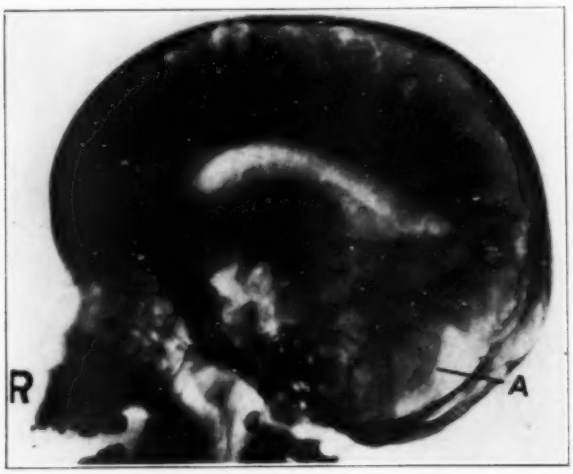

Fig. 30.—Encephalogram of a boy, aged 3½ years, who was drowsy and who refused to talk; hemiplegia followed birth trauma (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. Kwan. The observations indicated slight brain atrophy in the frontal and parietal region but the interesting feature was the large collection of air in the posterior fossa at *A*, which was regarded as evidence of cerebellar atrophy.

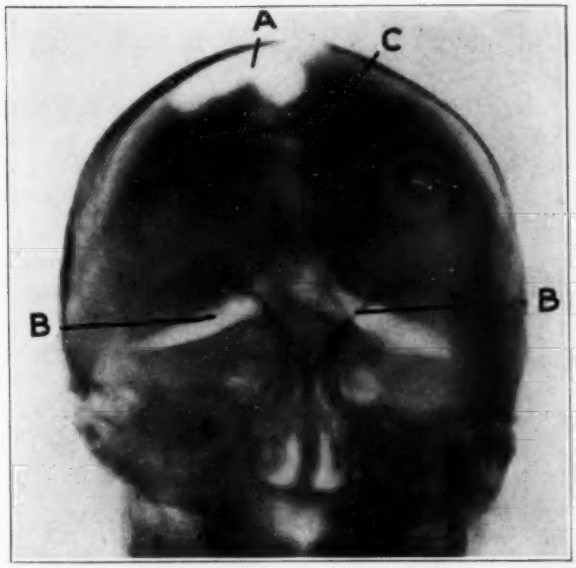

Fig. 31.—Encephalogram of a male infant, aged 1 year, in which case the diagnosis was microcephaly; there was failure to develop (service of Dr. Temple Fay, Episcopal Hospital). The encephalogram was made by Dr. Fay and Dr. R. S. Bromer. It indicates a marked aplasia or atrophy of the brain in the left frontal and parietal regions (*A*). The ventricles are not filled. The cisterna venae magnae cerebri is enlarged (*B*). The absence of subarachnoid markings at *C* may be due to a plastic arachnoiditis indicated by the absence of visible subarachnoid pathways.

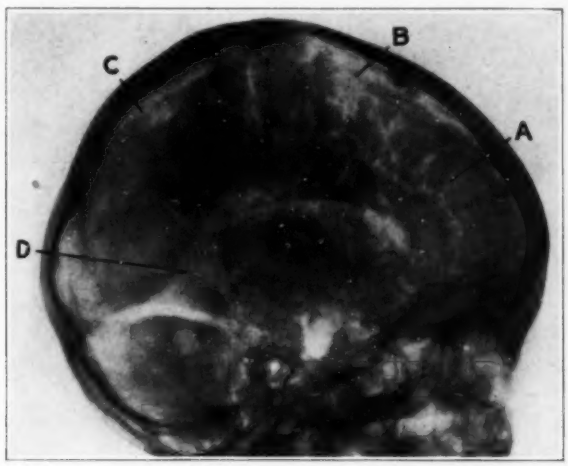

Fig. 32.—Encephalogram of a girl, aged 9, in whom the clinical diagnosis was post-traumatic epilepsy, who had had an injury six years before (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. James Gardner. The encephalographic observations show enlargement of the subarachnoid spaces in the frontal, parietal and occipital regions (*A, B* and *C*). The typical tent-shaped appearance of the cisterna venae magnae cerebri is clearly visible at *D*. The conclusion is: a moderate degree of brain atrophy, associated with post-traumatic epilepsy.

of the ventricles is explained possibly by the fact that withdrawal of fluid by the lumbar route causes a rupture of the thin membrane, which in turn allows the air to enter the ventricles.

There is still another encephalographic observation that has been attributed to an error in technic, that is, the filling of only one lateral ventricle. Except in the presence of strong clinical data and a displacement of the midline structures, this is always regarded as error in technic due to insufficient manipulation. A roentgenogram made the next day usually shows a filling of the other ventricle.

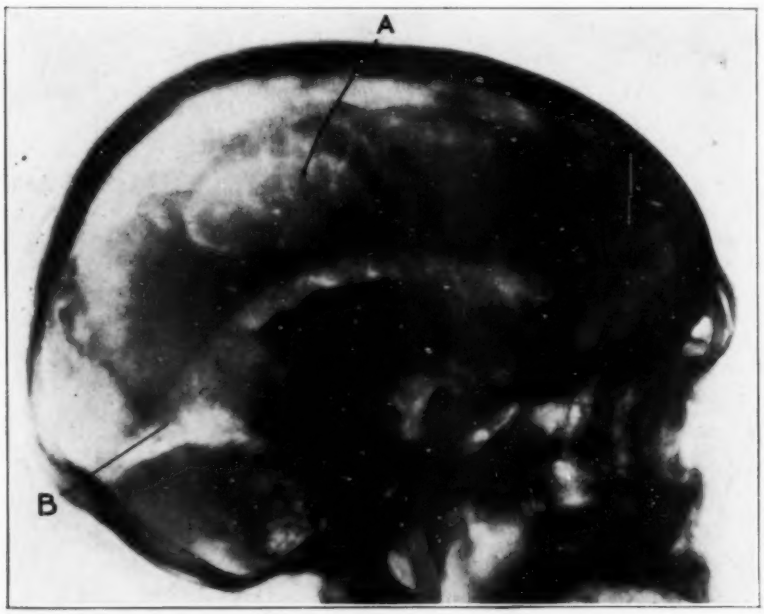

Fig. 33.—Encephalogram of a man, aged 30, in whom the diagnosis of posttraumatic epilepsy had been made (service of Dr. Temple Fay, Episcopal Hospital). The encephalogram was made by Dr. Fay and Dr. Bromer. The observations in the lateral view are enlarged subarachnoid pathways in the frontal, parietal and occipital regions. The large defect of the previous operative opening is clearly seen at *A*. The enlarged cisterna venae magnae cerebri is clearly visible; 215 cc. of fluid was drained from this patient.

Encephalograms should be made within an hour after the introduction of the air, the patient having been kept in the erect posture with the head in the midline. Otherwise, most peculiar observations and errors in diagnosis will be made. I believe that the air, which is subarachnoid at the time of the introduction, enters the subdural space, whereon the convolution markings are lost, and therefore the sooner the roentgenograms are made the better the result will be.

ENCEPHALOGRAPHIC OBSERVATIONS IN THE CONVULSIVE STATE

The essential encephalographic observations in the convulsive state are atrophy of the brain and arachnoiditis.

I have already described the encephalographic observations in the various stages of brain atrophy, but I did not discuss the types and possible causes. Roentgenologically, it is possible to distinguish between two large groups of atrophy: the superficial, presumably due to pressure, and the deep, which is ascribed to a lesion within the cortex.

I have attempted to classify atrophy of the brain into three groups, depending on the possible etiologic factors.

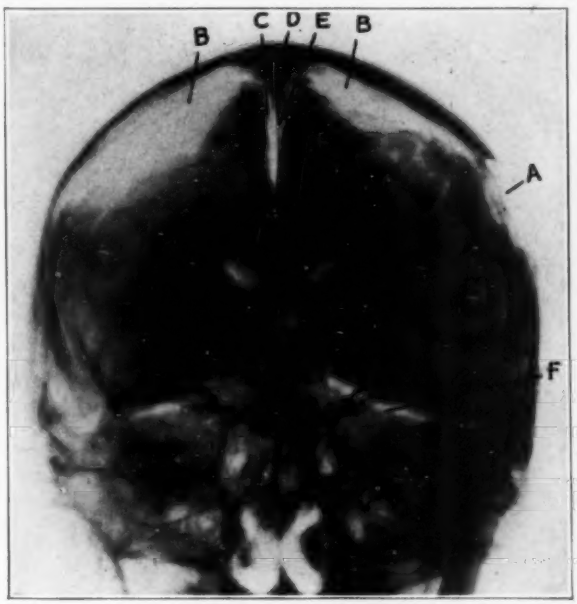

Fig. 34.—Anteroposterior view of same patient as in figure 32. The operative opening is seen at *A*. Note the bilateral cortical atrophy at *B*, without deformation of the ventricles. The cortical atrophy is more marked on the side opposite to the site of injury. The interhemispheric air can be seen at *C*, clearly defining the longitudinal sinus *D*, and the falx cerebri *E*. The cisterna venae magnae cerebri is clearly visible at *F*. The conclusion is: marked brain atrophy in a case of post-traumatic epilepsy.

1. Birth trauma: In this group I examined a number of babies and young children from 3 months to several years of age. I was astounded to see what was regarded as marked aplasia or possibly pronounced atrophy of the cerebral cortex, and in some cases actual cerebellar atrophy as well. In still others one could see evidence of atrophy or aplasia in the region of the insula of Reil. One can scarcely visualize the degree of aplasia or possible atrophy that is present within three months after

birth. If these interpretations can be accepted as correct, definite information can be obtained and a more scientific prognosis may be rendered.

Of the infants and young children that were studied, very few had all of the cerebrospinal fluid drained from the canal. Children are poor risks, and the procedure has to be performed under an anesthetic, all of which tends to make the procedure more dangerous.

The typical encephalographic observations are: There is beginning atrophy or aplasia of the frontal lobes, indicated by the increased size of the subarachnoid pathways. The area next affected seems to be the parietal lobe in the region of the motor area (figs. 27, 28, 29 and 30). The atrophy extends toward the base, and finally one finds compensatory

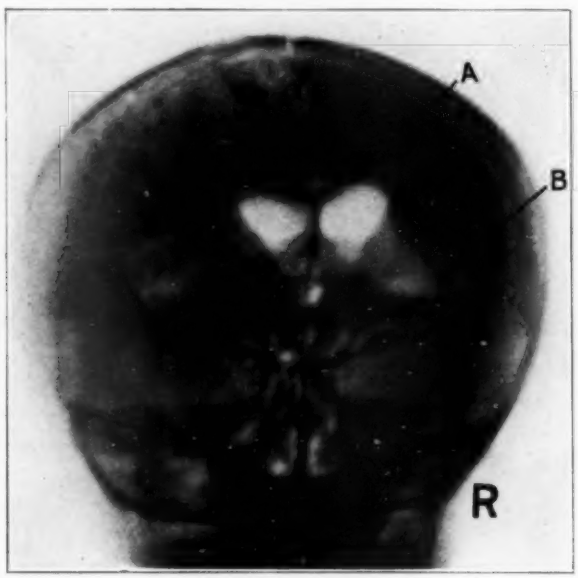

Fig. 35.—A boy, aged 3, in whom the diagnosis of traumatic epilepsy was made, fell one year before; generalized convulsions and paralysis of the left arm developed (service of Dr. Charles H. Frazier, University Hospital). The encephalogram was made by Dr. James Gardner. Note the absence of subarachnoid markings in the right side at *A*, which was regarded as evidence of plastic arachnoiditis. There is atrophy in the region of the insula of Reil at *B*. There is some deformation of the head, the left side being larger, and there is some shifting of the midline structures to the right. The lateral ventricles seem larger than normal. The diagnosis of plastic arachnoiditis was confirmed at operation.

pathways in the occipital region which are regarded as evidence of atrophy of the brain. These conditions may be unilateral or bilateral. The cisterna venae magnae cerebri is usually the largest compensatory space and is distinctly large in a number of the patients. Unfortunately, little information has been obtained thus far in regard to the ventricles

owing to the absence of drainage. Usually about 50 cc. of fluid is removed in these patients (fig. 31). As this amount of fluid does not drain the cerebrospinal canal, I believe this to be another evidence of aplasia or atrophy of the brain. In some of the patients subarachnoid pathways may be enlarged markedly on one side and may be absent on the other. When an encephalogram demonstrates these conditions, I believe that they are indicative of atrophy of the brain or aplasia on one side and plastic arachnoiditis on the other (fig. 31).

2. Post-Traumatic: I studied a large number of cases in this group. Some of the patients had a history of severe injuries to the head; others

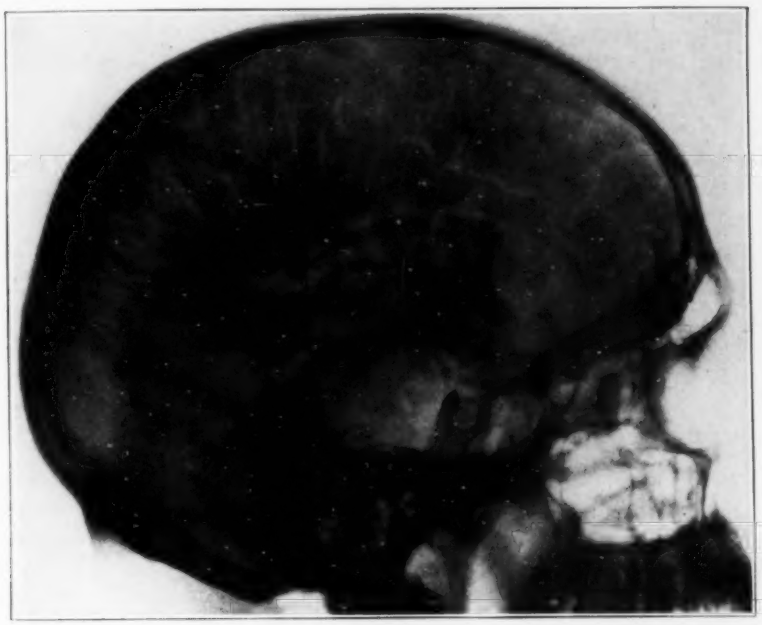

Fig. 36.—A man, aged 23, in whom the diagnosis of idiopathic epilepsy was made, had suffered from carbon monoxide poisoning four years before (service of Dr. Alfred Stengel, University Hospital). The encephalogram was made by Dr. Temple Fay. The encephalographic observations were: an increase in the size and number of the subarachnoid pathways in the frontal, parietal and occipital regions which were regarded as indicative of beginning atrophy of the brain.

had injuries to the head with depressed fractures, some causing the focal type of convulsive seizures; a third group were examined several years after the operative removal of a tumor of the brain and returned for observation because of jacksonian convulsions.

The encephalographic observations in this group are those of atrophy of the brain or arachnoiditis or the combination of the two processes. In the early cases, one can see clearly an increase in the size of the

subarachnoid pathways in the frontal region. This seems to be the first area to suffer; at least, changes are found here most frequently. In more advanced cases, the subarachnoid pathways are increased in size in the parietal region over the motor area. The next most frequent abnormality is the enlargement of the cisterna venae magnae cerebri, and finally the subarachnoid markings in the occipital region enlarge. Possibly these changes can be regarded as compensatory (fig. 32). In the most advanced cases there is almost a complete disappearance of the subarachnoid markings in the frontal and parietal regions. The pathways are replaced by large collections of air between the surface of the

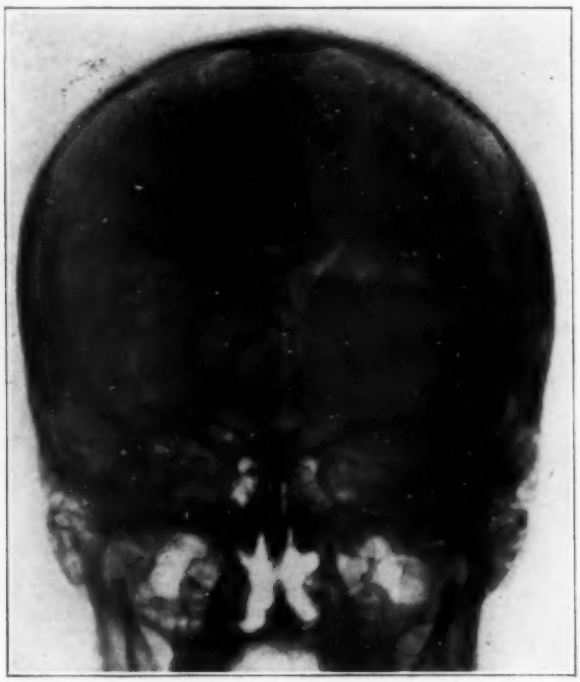

Fig. 37.—The anteroposterior view of the same patient as in figure 36. Note the increased size of the subarachnoid pathways. The convolutions can be outlined. One ventricle is not filled, which is regarded as an error in technic.

cortex and the inner table of the skull. The basal cisternae are also large, and in some cases there may be cerebellar atrophy, indicated by large collections of air surrounding the cerebellum (figs. 30, 33 and 34).

Arachnoiditis is the interpretation in those encephalograms in which there is an absence of subarachnoid pathways, provided errors in technic and an associated atrophy of the brain can be excluded. The arachnoiditis may be localized over the motor area and be sufficient to be the only positive observation in jacksonian epilepsy. This observation has

been confirmed at operation a number of times, and I feel certain that arachnoiditis is at least a part, if not the cause, of some of the focal manifestations. The arachnoiditis may be unilateral, bilateral, localized or associated with atrophy of the brain (fig. 35). In my experience, arachnoiditis is more often associated with jacksonian epilepsy.

3. Idiopathic: In this group were placed all cases of atrophy of the brain that have no known cause. In these the cause may be birth trauma, some inflammatory process or possibly a hereditary or congenital deficiency of the pacchionian bodies and subarachnoid villi, or anomalies in the venous drainage system of the brain as pointed out by Swift (1929). The atrophy observed in these cases does not vary from that seen in the post-traumatic group.

The atrophy evidenced by large subarachnoid pathways usually is seen first over the frontal lobe. In other cases the pathways are enlarged over the frontal and parietal regions (figs. 36 and 37). In the advanced cases the basal cisternae are enlarged, and compensatory pathways may be seen over the occipital region.

I observed one case of extensive atrophy for which there was no cause and no history of convulsions. This makes one think that the amount of atrophy may not have any relationship to the convulsive state other than that it is a part of the pathologic process (fig. 9). I have made no effort thus far, from the roentgenologic aspect, to correlate the amount of atrophy, the number of convulsive seizures and their duration.

COMMENT

Some form of atrophy of the brain has been present in all cases of the convulsive state that I have studied. The atrophy seems to be limited to the cerebrospinal fluid pathways and in order of the frequency of occurrence, the following areas seem to be affected: the frontal region, the parietal region, the basal cisternae, the cisterna venae magnae cerebri, the occipital lobes, the temporal lobes and the cerebellum. In severe cases of atrophy, all of these areas may be involved. Atrophy of the brain, or possibly aplasia, is present to a marked degree in infancy, as early as at 3 months of age.

I feel sure that slight and even marked atrophy may occur without convulsive seizures; mental deficiency is present, however. I am not prepared to state how atrophy of the brain is related to the convulsive state; I make only the observation that it has been present in the series of cases of epilepsy studied by me.

That atrophy is present is also shown by the large withdrawals of cerebrospinal fluid in some cases. In these cases one is always able to make encephalographic observations that are ascribed to atrophy of the brain. The atrophy does not follow the vascular plan.

Arachnoiditis is most frequently found in the focal type of epilepsy.

CONCLUSIONS

The procedure of encephalography is safe, and under the conditions outlined in the text reveals a pathologic process that otherwise could not be demonstrated. It is of greatest value in differentiating the type of pathologic process to be found in the convulsive state. Atrophy of the brain can be differentiated from plastic arachnoiditis. A diagnosis of porencephaly can be made. Tumors of the brain causing jacksonian convulsions can be demonstrated.

An effort has been made to standardize the technic of drainage of the cerebrospinal fluid and introduction of the air and the interpretation of the roentgenologic aspects. If this is possible, one will be able to follow a given case from year to year and demonstrate whether or not the pathologic process is stationary or progressive; thus there will be a check on the value of whatever treatment is instituted.

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NEUROSOMATIC DETERIORATION IN EPILEPSY*

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Report of Cases
Comment
Common Symptomatologic Pattern of Neurosomatic Deterioration in Chronic Epilepsy
Symptomatologic Variants of the Neurosomatic Deterioration in Chronic Epilepsy
Residual Syndromes (Sequelae) of the Primary Cerebral Lesion and the Symptom-Complex of Progressive Neurosomatic Deterioration
Akinetohypertonic and Pyramidal Syndromes as Shown in Advanced Neurosomatic Deterioration
Pseudobulbar Phenomena in Advanced Deterioration; Neurosomatic Deterioration in Epilepsy and in Presenile or Senile Arteriosclerotic Parkinsonism
Results of a Neurologic Survey of a Large Number of Average Institutional Cases of Epilepsy
Summary

The progressive changes that develop in many epileptic patients in the course of time constitute what is generally called deterioration. Indeed, in the course of years, many persons with epilepsy fail both mentally and physically. These essentially progressive mental and physical changes should not be considered independently of each other; no doubt they constitute, at least clinically speaking, one disease process. In spite of recent advances in clinical neurology little attention has been given to the progressive neurosomatic impairment in chronic epilepsy, i.e., the progressive impairment in the physical and not the psychic sphere. We feel justified therefore in presenting neurologic observations made along these lines in a large number of cases.

We shall report first a series of typical case histories illustrating the characteristic organic neurologic changes that develop in the course of the deterioration in chronic epilepsy. We shall discuss then the common points of these observations, the relationship between various symptomatologic components of neurosomatic deterioration, and the probable nature and localization of underlying pathologic processes. Finally, we will give a brief statistical account of the result of the neurologic survey of a large number of average institutional cases of epilepsy.

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* Read before the Association for Research in Nervous and Mental Diseases, New York City, Dec. 27, 1929.
* From the Monson State Hospital.

REPORTS OF CASES

CASE 1.—*Extreme muscular rigidity developing after status.*

History.—Wayne St., a boy aged 14 years, with unimportant family history, was born at full term after a normal labor. He began to walk at 15 months and talked at 18 months of age. Teething commenced at the average age and was not difficult. He had no convulsions in infancy. He developed well and at 5 years of age went to school. At 6, he had measles, during which he had his first convulsion. He recovered from the measles without other complications but continued to have convulsions which, in the course of time, grew more frequent; the mental condition became impaired and he had to leave school at the sixth grade. In 1923, when 10 years of age, he was admitted to the Monson State Hospital. He had numerous and typical grand mal attacks, varying from two to six every twenty-four hours.

Neurologic Examination.—On admission, the neurologic condition was normal.

Course.—In time, the attacks became less frequent but showed a tendency to occur in series; on several occasions he developed status. Mental deterioration progressed rapidly. Two years after admission, slowness of movements, lack of facial expression and some degree of generalized muscular rigidity were noted. In August, 1926, when aged 14, he developed a severe condition of status which lasted for several days; he was completely unconscious; the temperature was high (from 104 to 105 F.); the pupils were immobile; all superficial and deep reflexes were abolished. Between the convulsions, which occurred every ten or fifteen minutes, the muscles were completely relaxed. Ten days later, he regained consciousness and was able to get up. The condition then was much changed; he had a coarse tremor in both hands; his face was inexpressive and masklike, and he was drooling; on passive movements all the extremities were rigid; the head was bent down; the trunk inclined forward; the arms and legs were adducted and flexed; the hands and fingers were in the parkinsonian position. Movements were extremely slow; in walking associated movements in the arms were absent. The voice was very weak; speech was monotonous and so thick as to be hardly understandable. Segmental power was not much diminished. Passive movements showed pronounced generalized waxy rigidity, predominating on the left side. A cog-wheel phenomenon was present in the arms. Tonic postural reflexes and reaction of the antagonists were exaggerated on both sides, particularly on the left. The tendinous reflexes were active, abrupt, of short amplitude and hypertonic. The patellar reflexes were particularly rigid; on eliciting the patellar reflex, the hamstring antagonistic contraction was very intense, especially on the left side. The abdominal reflexes were present on both sides. There was no clonus. The plantar reflexes were dull and sluggish; the response on both sides was of flexor type. Reflexes of defense were absent. Pinching the skin did not produce any reaction on the part of the patient, either motor protective or emotional. If asked how it felt, he would answer, "It is sore." He recognized hot from cold, and pin prick from a touch with a dull point. The pupils were equal and reacted normally. There were no nystagmus and no intention tremor. There was tremor in the tongue. The tremor in the hands and fingers was rhythmic and continuous, not increased but rather diminished by voluntary movement. The patient remained in this condition for ten days, during which he had no convulsions; then status again developed with excessive hyperthermia (107 F.). He died two days later without recovering consciousness. Permission for an autopsy was refused.

CASE 2.—*Progressive muscular rigidity developing in the course of chronic epilepsy.*

History.—Charles S., aged 29, whose family history was without significance, was born at full term after a normal labor. He walked and talked at 14 months; teething commenced at 8 months and was not difficult. He had no convulsions in infancy. Measles occurred when 3 years of age without complications; he had no other diseases of childhood. He was in good health up to the age of 12 years when, without evident cause, he had his first convulsion. About the same time, progressive changes of personality were noted. He showed mischievous behavior, indifference to the moral and disciplinary influence of his elders, lack of affection for his parents, and an inclination to be cruel to younger children. The epileptic attacks grew more frequent. When 15 years of age, he was admitted to Monson State Hospital.

Examination.—On admission, the neurologic picture was normal. Mentally, he presented a picture suggestive of dementia praecox of the hebephrenocatatonic type: incoherence of mental associations, indifference and violent impulsions, with periods of catatonic immobility. Owing to his unusual physical vigor and violent and impulsive homicidal reactions, he was difficult to care for and probably this was the motive of the castration which was performed.

Course.—In the following years, convulsions grew more frequent and rapid deterioration, both mental and physical, set in. Figure 1 shows a photograph of the patient taken at the time of admission. Figure 2 shows him in his present state. He is much demented; his speech is monotonous, stuttering and poorly articulated. He is completely indifferent to the environment. His face lacks expression; at times he smiles or gives vent to explosive laughter without any obvious reason. His mouth is open most of the time and saliva drools on his clothes. All the body is rigid. The head and trunk are bent forward, the arms and legs flexed. The hands and fingers are kept in a rigid position. Rhythmic coarse tremor is present in the hands (note the right hand in fig. 2) and fingers. Movements are slow; automatic movements in the arms when walking are absent. Muscular rigidity is very pronounced when testing passive movements. A cog-wheel phenomenon is present in both arms. The reactions of antagonists and tonic postural reflexes are exaggerated. Tendinous reflexes are hypertonic. The patellar jerk is short and abrupt, with a tendency to fix the leg immobile in the extension phase; the hamstring antagonistic contraction is very strong. Muscular power is good. The abdominal reflexes are present. The plantar reflexes are dull and sluggish; a flexor response is obtained on both sides. There is no clonus. No other symptoms of the pyramidal series are found. The reflexes of defense are diminished. There is complete emotional indifference to painful stimuli; for example, pinching of the skin of ankles. The pupils are equal, and react to light and in accommodation. There are no cerebellar symptoms. On gross tests the principal forms of sensation are undisturbed. Convulsions on the whole are less frequent than in the previous years.

CASE 3.—*Progressive muscular rigidity of Parkinson's syndrome type developing in a case of late epilepsy.*

History.—Louis C., aged 50, whose family history was without significance, when 32 years of age began to have epileptic fits, at first light petit mal attacks, later complete epileptic convulsions. They grew more frequent so that, at times, he would have several fits daily. His mental and physical condition grew slowly worse. In the course of fifteen years the condition became so much worse that he was unable to support himself. At the age of 47, he was admitted to the Monson State Hospital.

Examination.—On admission the neurologic examination gave negative results. The tendon reflexes were present; the pupils reacted well. Mentally, he was considerably deteriorated, slow and apathetic.

Course.—Since admission, the convulsive attacks have steadily grown less frequent; for the last year, from May, 1927, to May, 1928, he had not been seen in a severe convulsion, but he had light attacks when he lost consciousness for a moment, sometimes fell ("tips on one side") without convulsion, regained consciousness immediately and rose again. During hospitalization, progressive changes have been observed, not so much in the mental condition, which remains

Fig. 1.—Patient in case 1 at the age of 15.

about stationary, but in the physical condition. Gradually, he developed the following clinical picture (fig. 3); he became very slow in movement; the body attitude became rigid, with flexion of the head and trunk; slight propulsion of body occurred, particularly when walking. The arms are flexed and adducted, the hands in a characteristic position, thumb and index together; "pill-rolling" tremor is observed at times; a fine tremor of the fingers is always present; when walking, associated movements are absent; the steps are short-gait "trotting"; the face is masklike and inexpressive; the glance is fixed, though the eye movements are free and contrast with the immobile attitude of the head and the fixed facial expression; the voice is very low and monotonous, the speech dragging; passive movements are heavy in all segments; the cog-wheel sign is exquisite in both arms; tonic postural reflexes are exaggerated; reaction of the antagonists is exaggerated.

In records for 1926 and 1927, it was said that the tendon reflexes were hypertonic; in later records they were qualified as sluggish and diminished. At the present time, the left achilles and left patellar reflexes are not obtainable. The tendon reflexes are active in the upper extremities. About the end of 1927, there was noted a sluggishness of the pupillary reflexes to light, but this was not constant and

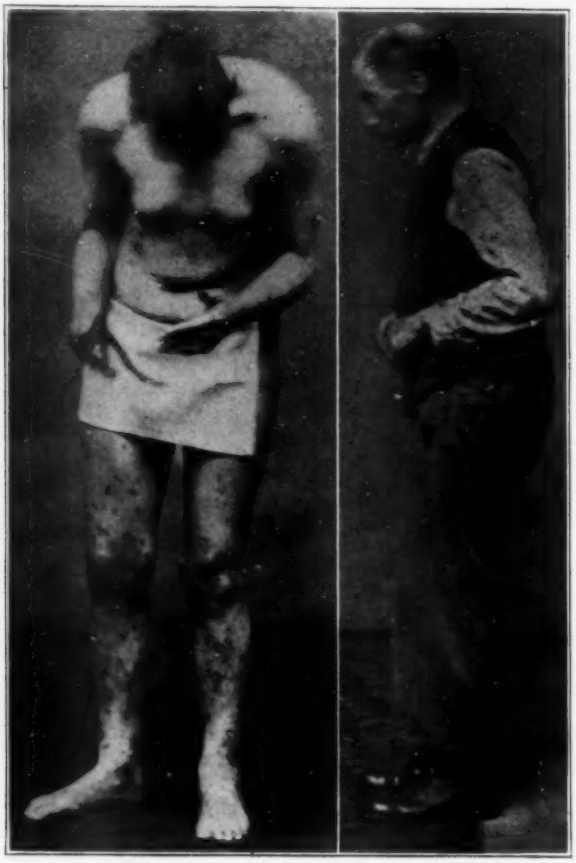

Fig. 2 Fig. 3

Fig. 2.—Same patient as in figure 1, at the age of 29 years, showing his present condition. Note the flexion posture of the head, trunk and extremities and rigid position of the hands; tremor of the right hand is seen.

Fig. 3.—Patient in case 3, at the age of 49. Note the parkinsonian attitude of the body and the inexpressive face. General rigidity can be seen from the aspect of the patient.

at times the pupils contracted well to light on both sides. The abdominal reflexes are present. There is no clonus. The plantar reflexes are dull and sluggish; the response is flexor on both sides. No other symptoms of the pyramidal series are present. Reflexes of defense are diminished; there is no motor reaction and very

slight emotional reaction on pinching the skin of the ankles. There are no cerebellar symptoms. No Romberg sign is present. Vibration sense and position sense are preserved. There are no sensory disturbances. The Wassermann reaction of the blood and spinal fluid has always been negative. The spinal fluid shows a normal content of proteins; there is no lymphocytosis. The blood pressure, in 1925, was 124 systolic and 78 diastolic; in 1928, 100 systolic and 66 diastolic. The urine is free from albumin and sugar.

CASE 4.—*Pseudobulbar paralysis with rigidity, tremor and bilateral pyramidal symptoms developing at the age of 45 in a feebleminded person with chronic epilepsy.*

History.—Thomas M., aged 61, whose family history was unknown, had had epileptic fits since the age of 12. About the same time he became an inmate of a state institution for the feebleminded and remained there until the age of 40. In later years, the epileptic convulsions became very frequent and on the background of congenital feeblemindedness mental deterioration developed. In 1908, he was transferred to the Monson State Hospital where he has remained since. He had frequent convulsions and about five years later, when he was from 45 to 47 years of age, he became much deteriorated both mentally and physically; this condition progressed slowly but steadily. He never had any apoplectic insults; the blood pressure was always normal. During the last ten years, the condition has remained as it is at the present time, except that he has had no more severe convulsions, but only light attacks when he seems dizzy, stumbles, and sometimes falls, without having true convulsive fits.

The present condition, which has not changed for the last two or three years, is highly characteristic (figs. 4 and 5). The head droops on the chest, the lower jaw is relaxed and the mouth open; he drools a great deal. The face is immobile and inexpressive; spasmodic laughing and crying are easily induced; the arms are flexed at the elbows; both hands are rigid and extended at the wrists; the fingers are flexed on the palms at the first phalanges; the distal phalanges are overextended (fig. 5), the thumb and index finger in apposition; there is tremor of the head and hands; pill-rolling movements of thumb and index finger are present. The gait is rigid, slow and trotting; the steps are short and unequal as the left leg is more rigid and does only a half step. On passive movements, rigidity of the flexors and extensors is observed. The reaction of the antagonists is very intense, more so on left side. Tonic postural reflexes are not well sustained on the right ankle; they are better sustained on the left. The tendon reflexes are hypertonic, with intense antagonistic contraction of the hamstrings when eliciting the patellar reflexes. There is no clonus in the left foot; a few beats are obtained on the right. The plantar reflex on both sides is extensor in type. Reflexes of defense are exquisitely exaggerated on both sides, more so on the right. There is marked hyperalgesia on pinching the skin of the ankles, with excessive emotional reaction and spasmodic crying. Speech is thick, nasal and dysarthric, with a tendency to retail the words at the end of expiration, repeating one word or a syllable several times. Mastication is difficult on account of missing teeth and weakness of the jaw muscles. Swallowing is difficult, with frequent choking and return of food through the nose. The left pupil reacts to light; the right eye was enucleated several years ago following a traumatism.

CASE 5.—*Latent left-sided infantile hemiplegia followed by epilepsy; progressive rigidity, development of pyramidal symptoms on the right side; eventually onset of pseudobulbar symptoms.*

History.—Doris P., aged 10, whose family history is without significance, was born at full term; there were no birth complications. Teething began at the end

of the first year and was associated with a few convulsions. The child walked and talked at the end of the first year. She was in good health up to the age of 5 years when, without evident cause, she had a convulsion, following which the left side was paralyzed. The paralysis was not severe and cleared up a few weeks later, but she continued to have convulsions which grew more frequent. Gradually, mental impairment set in. When 8 years of age she was admitted to Monson State Hospital.

Examination.—On admission she appeared dull and apathetic, but not demented. A peculiar tendency to keep the head down on the chest was noted. Movements

Fig. 4.—Patient in case 4, at the age of 61. Note the flexion attitude of the head and upper extremities and rigid posture of the hands and fingers.

were slow when walking; the arms were kept immobile along the sides of the body. The gait was trotting, with short steps and slight dragging of the left leg. A left-sided hemiplegia was present. The left arm and leg were somewhat weaker than the right. There were slight choreo-athetoid movements in the fingers and toes on the left. The tendon reflexes were more active on the left side. The abdominal reflexes were diminished on the left. A Babinski sign was present in the left foot; a pronator sign in the left forearm, and a combined flexion sign on the left. Reflexes of defense were exaggerated on the left, normal on the right.

Course.—Epileptic attacks continued to be frequent and she showed a tendency to develop serial attacks with intervals of several weeks. In the interim she

would have frequent petit mal fits. At the end of one year after admission, she developed a severe condition of status. Following this, mental enfeeblement, slowness of movements and signs of muscular rigidity, especially on the right side, made rapid progress. It was noted that the head drooped still more (fig. 6). The mouth was kept open; she drooled profusely and, when eating, food often returned through the nose. Speech was thick and whispering, so that she could hardly be heard. The facial expression became more dull and inexpressive. Pyramidal symptoms, though always more pronounced on the left side, appeared also on the

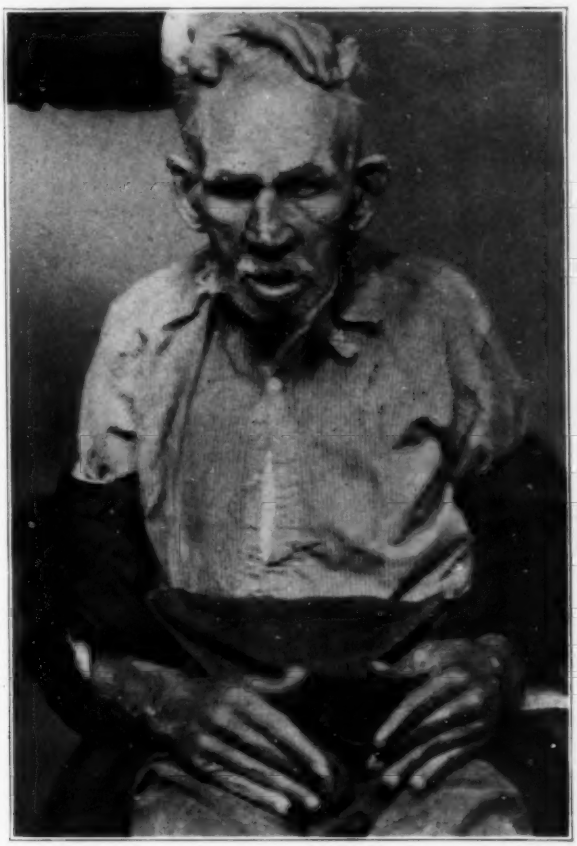

Fig. 5.—Same patient as on figure 4. Note the pseudobulbar facial expression and the posture of the hands and fingers. Tremor of the hands can be seen.

right side. A bilateral Babinski sign was recorded. Reflexes of defense became exaggerated on both sides. Spontaneous voluntary movements became much diminished. The involuntary choreo-athetoid movements almost disappeared. She remained in bed most of the time. She had a tendency to double up in bed, the legs flexed on the thighs and the knees drawn up under the chin. On passive extension of the legs a slight contracture of the flexors was noted. Muscular rigidity became pronounced in the trunk and extremities. Tonic postural reflexes

became exaggerated on the right side; they were less evident on the left. She continues to fail, with periods of relative improvement alternating with periods of further impairment when she remains bedridden for weeks.

CASE 6.—*Progressive rigidity, bilateral pyramidal symptoms, symptoms of pseudobulbar type and flexion contracture of the lower extremities, developing in the course of chronic epilepsy.*

History.—Joseph McG., aged 15, whose family history is without significance, was born at full term without birth complications. At 4 months of age, when cutting the first teeth, he began to have convulsions and continued to have them there-

Fig. 6.—Patient in case 5, at 10 years of age. Note the flexion posture of the head and rigid posture of the hands. Latent left-sided hemiplegia can be noticed by drooping of the left shoulder and posture of the left ankle and left hip joint.

after. He cut his teeth, walked and learned to talk at the average age. After the first, year, the convulsions increased in number. Mental development became retarded. On account of this and numerous convulsions he never went to school. In October, 1923, when 12 years of age, he was admitted to Monson State Hospital.

Examination.—On admission a psychometric test gave a mental age of 4 or 5 years. Physically, he appeared well developed. A neurologic examination gave negative results. Movements were free; coordination was good. The reflexes were normal. There was no paralysis and no contractures.

Course.—The boy continued to have frequent epileptic attacks, and during the year 1924 had on an average from fifteen to twenty grand mal convulsions per month. Nevertheless, the physical condition remained satisfactory. He was active and played with other children. Gradually, after 1924, the grand mal convulsions grew less frequent and showed a tendency to occur in series. In 1925 and 1926, he had on an average ten fits a month. In 1927 and 1928, the average number of attacks fell to four or five per month. He continued, however, to have attacks of petit mal with few convulsive movements. Since 1926, at the age of 12, mental and physical deterioration has made rapid progress. The patient has become apathetic. His face looks like that of an old man. He keeps the head flexed on the chest, the trunk bent forward, the arms and legs flexed. Gait has become awkward. Considerable muscular rigidity has been noted in all extremities. He drooled a great deal. The tendon reflexes were hypertonic. Reflexes of defense appeared to be exaggerated with a strong emotional reaction. A suggestion of a Babinski sign on the left side was noted. The condition continued to grow worse, with periods of apparent improvement followed by further impairment. Rigidity progressed; walking and even standing became difficult. Since 1927, he has been confined to bed most of the time.

In 1927 (July-August), neurologic examination showed: pronounced flexion rigidity (fig. 7); a characteristic rigid attitude of the hands and fingers; coarse tremor of the hands; tremor of the tongue. The tendon reflexes were exaggerated and of low threshold; the patellar jerk was polykinetic and of short amplitude and abrupt, with intense antagonistic contraction of the hamstrings. There was clonus of both feet. A bilateral Babinski sign was present. The cog-wheel sign was present in both arms. Reaction of the antagonists was highly exaggerated. Tonic postural reflexes on the ankles were, on the contrary, diminished. Reflexes of defense were exquisitely exaggerated on both sides, with intense flexion contracture of the lower extremity. Passive movements in the upper extremities showed resistance of both flexors and extensors; in the lower extremities contracture of the flexors distinctly predominated. At present, the patient is confined to bed, where he lies with both lower extremities drawn up and the thighs in contact with the abdomen, the heels touching the buttocks, the ankles and toes in plantar flexion (fig. 8). Passive extension of the leg increases the contracture of the flexors. Walking is impossible without assistance. Standing is difficult. Since the summer of 1927, changes in speech, mastication and swallowing have been noted. Speech became nasal and thick; the patient pronounces words at the end of an expiration, as if shouting out. The face became masklike and inexpressive, except when crying. He drools profusely. Mastication is slow and difficult. The act of swallowing is often complicated by choking, coughing and rejection of food through the nose. Since the end of 1927, signs of pulmonary tuberculosis have been present. He was transferred to a special ward. For the last year the condition has remained stationary.

CASE 7.—*Progressive rigidity, contracture of the lower extremities, pseudobulbar symptoms, with further evolution into a typical cerebral flexion-paraplegia with severe tendinous retractions, developing in the course of chronic epilepsy.*

History.—Raymond P., aged 26, whose family history is without significance, was born at full term, without birth complications. He was slow in development; he learned to walk at 2 years, and began to talk at 3 years. Physically, he was in good health up to the age of 5, when he fell from a wagon and injured his head. He was in bed for several days, but recovered completely and had no paralysis. Shortly afterward, he had the first convulsion. He went to school at 5, but

completed only the first grade and on account of convulsions had to be kept at home. At 11 years of age he was admitted to Monson State Hospital as a feebleminded epileptic patient.

Examination.—On admission, the physical condition, apart from the epileptic convulsions, was satisfactory. Neurologic examination gave negative results. There was no evidence of paralysis.

Course.—The condition remained satisfactory for several years afterward. At 15, he was able to play football and was vigorous and active (fig. 9). The attacks

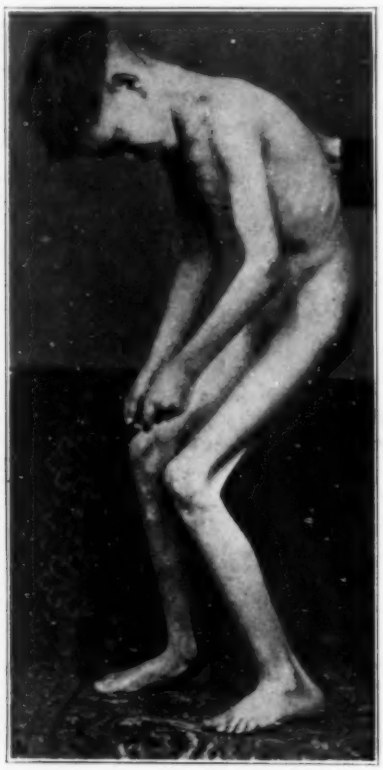

Fig. 7.—Patient in case 6, at the age of 15. Note the flexion posture of the head, trunk and extremities, and contracture of the flexors in the lower extremities.

were almost exclusively nocturnal. When 17, the fits increased in number and the first changes in the general condition were noted. He became apathetic and slow; this grew more pronounced in the course of time. He gradually developed characteristic changes in general posture, with a flexion attitude of the body and general rigidity. The gait became difficult and awkward. In the course of three years, he became a permanent bed patient; at the same time, the mental condition failed greatly. Speech became dysarthric; thick and poorly articulated, at first, it later became incomprehensible and eventually he ceased to speak at all; at the

present time he only groans if disturbed. Difficulty of mastication and swallowing was noted and this grew worse; at the present time he has to be fed fluids as he chokes easily. Since he became confined to bed, the contracture of the lower extremities has become more severe and, gradually, tendinous retractions have set in so that during the last four years the legs have become completely immobilized in a flexion position (fig. 10). The head and upper extremities show considerable rigidity; notwithstanding this he can move the head and arms fairly well. On the contrary, the trunk and lower extremities are doubled up, the knees drawn under the chin, the legs flexed on the thighs, the ankles and toes in plantar flexion. Tendinous retraction makes passive movements impossible in the ankle joints and knees, and greatly reduced in the hip joints. His face is striking by reason of its immobile rigid expression, with the mouth half open. The eyes are usually closed, but if stimulated he opens them and it is seen that the eye movements are free; the pupils react to light. Continuous rhythmic lateral movements of the

Fig. 8.—Same patient as in figure 7. Note the flexion attitude of the lower extremities.

eyes are present; the optic disks are pale; otherwise the eyegrounds are normal. Tendon reflexes in the upper extremities are rigid and of short amplitude; in the lower extremities they are not elicitable. The plantar reflexes are not elicitable because of retraction of the toes of both feet. Extreme rigidity of the abdominal walls does not permit the abdominal reflexes to be elicited. Reflexes of defense are exaggerated. Pinching the skin of the ankles produces distinct contraction of the flexors of the thigh, though the resulting movement is reduced to a minimum by tendinous retractions. Also, slight tickling of the sole of the foot produces accentuation of the flexion contracture of the thigh on the abdomen; the toes, ankle and knee joints remain immobile. The patient continues to have frequent nocturnal convulsions. The convulsive movements are confined to the head, upper part of the trunk and upper extremities. The lower extremities remain immobile. The patient does not react when called by name; he twitches slightly on a sudden noise; otherwise, he remains in bed quiet and motionless.

CASE 8.—*Progressive muscular rigidity, spasmodic laughing, bilateral pyramidal symptoms, spasticity and tendency to flexion contracture of the lower extremities developing in chronic epileptic person with left hemiplegia.*

History.—M. S., a woman, aged 40, whose family history is unknown, had had epileptic fits since childhood and was paralyzed on the left side of body at the time when she began to have convulsions. She was admitted to Monson State Hospital when 18, as a feebleminded epileptic patient.

Examination.—On admission, a left-sided infantile hemiplegia was found, with mild contracture of the flexors and pronators in the left upper extremity and with

Fig. 9.—Patient in case 7, at 14 years of age.

Fig. 10.—Same patient as in figure 9, at 26 years of age. Cerebral flexion paraplegia occurred in the course of deterioration, also dysphagia, tendinous retractions and trophic joint changes. Voluntary motility of the upper limbs is preserved. The patient was demented.

paralytic clubfoot on the left side. The tendon reflexes were exaggerated, and foot clonus and a Babinski sign were present on the left side. Weakness of the left side of the face was noted in the record. The mental condition was relatively good and remained so for several years afterward.

Course.—She was occupied as a helper on the ward and was actually useful as a worker. Soon after admission, a tenotomy was performed on the clubfoot with partial improvement in the gait. She was of pleasant appearance (fig. 11), neat in dress and orderly. However, as she approached her thirtieth year, mental and physical deterioration became more and more conspicuous. Together with recrudescence of epileptic convulsions, she had several periods of confusion and intense agitation. In the course of the following years, the mental condition necessitated transfer to a ward for demented patients. With the mental deterioration, neurologic changes developed and progressed. She became awkward and rigid in movements. Pyramidal symptoms appeared on the right side. Speech became dysarthric, the function of mastication and swallowing became impaired. Later, contracture of the flexors developed in both lower extremities. The present condition shows an unusually high degree of generalized muscular rigidity and extreme slowness and awkwardness of movements; there are flexion of the head on the chest, flexion of the trunk forward and flexion of the arms and legs when standing. Walking is impossible without assistance on account of rigidity of the lower extremities and retropulsion (fig. 12). A cog-wheel sign is present in the right arm. Contracture of the flexors and pronators in the left arm make passive movements extremely rigid and limited. The tendon reflexes are hypertonic on both sides, abrupt and of short amplitude. The patellar jerks on both sides show a pronounced tendency to fixation of the leg in the extension phase of the jerk, so that in repeating the taps one obtains a complete extension of the leg which remains in this position for from fifteen to twenty seconds and then slowly returns to the neutral position. Passive movements in the lower extremities show intense rigidity with contracture of the flexors on both sides, more pronounced on the left, hemiplegic side. The plantar reflex is extensor on both sides. There is no clonus of the foot on either side. The abdominal reflexes are not obtained. The reaction of antagonists and tonic postural reflexes is exaggerated, more on the right side. Reflexes of defense are abolished on both sides; no motor, or emotional reaction is obtainable when pinching the skin of the lower extremities. The face is inexpressive and masklike, and the mouth usually remains open. Spasmodic explosive laughter and crying are easily induced. The tongue is protruded slowly and incompletely. She drools a great deal. The patient is demented and unable to answer the most simple questions. She remains in bed or in a chair most of the time, the body doubled up, the head and knees brought together, the thighs drawn up on the abdomen. The propensity to the flexion attitude increases when she is in bed or lying down (fig. 13). Passive extension of the lower extremities in this position is opposed by contracture of the flexors. There is no tendinous retraction except in the plantar flexors of the left ankle.

CASE 9.—*Progressive rigidity, bilateral Babinski sign, exaggerated reflexes of defense, dysarthria, dysphagia, spasmodic laughing and crying, and tendency to flexion contracture of the lower extremities, developing in a chronic epileptic patient.*

History.—Eleanor K., aged 25, whose family history was unknown, was born at full term, without birth complications. She cut her teeth at the average age, began to walk at 11 months, talked at 1 year, and had no convulsions in infancy. She had measles at 8 months, mumps at 3 years and chickenpox at 4 years, without complications. She was in good health up to the age of 6, when she was taken ill and the condition was diagnosed as encephalitis. She recovered from this illness, but six months later began to have convulsions which continued thereafter

with varied frequency. Mental retardation appeared and in 1912, when 9 years of age, she was admitted to Monson State Hospital.

Examination.—Mentally, she was defective but physical examination gave negative results. The reflexes were normal. There was no evidence of motor disturbances.

Course.—She remained in the hospital for two years and, as the condition improved, was taken home. On the establishment of catamenia (aged 13 to 14), the condition became worse and in 1917, when she was 15, she was admitted for the second time (fig. 14). At this time the mental condition was worse. On

Fig. 11.—Patient in case 8, at the age of 22.

examination, for the first time a tendency to extensor response in the left foot was noted; however, on the whole, the neurologic examination gave negative results. Two and a half years later (1920), she returned home again and was readmitted for the third time in 1922. On this admission, mental deterioration was advanced, the patient being dull, slow and apathetic. An extensor response was present on the left; clonus was present on both sides and overactive tendon reflexes were recorded at that time. Since the last admission, the condition has slowly but steadily grown worse. The frequency of convulsions has remained about the same, with periodic variations up and down. On an average she had from five to ten, later from five to eight, convulsions per month. There were present: motor apathy and muscular rigidity; a flexion attitude of the trunk and lower extremities (fig. 15); spastic and rigid gait; a tendency to propulsion when walking; immobility of the face; drooling, and poor articulation of words.

Fig. 12.—Same patient as in figure 11, at the age of 40. Note the flexion posture, rigidity and retropulsion. Left infantile hemiplegia was present. The left clubfoot was partially corrected by operation.

Fig. 13.—Same patient as in figure 11. Flexion rigidity increased when in lying position, when in bed the legs are always drawn up.

The present condition, nineteen years after the onset of epilepsy, is one of a very deteriorated epileptic person. Generalized muscular rigidity became well developed and is distinctly more pronounced in the trunk and at the root of the extremities than in the distal segments. Passive movements are heavy with a cog-wheel phenomenon in both arms. Flexion contracture is pronounced in the lower extremities, with a tendency to a "clasp-knife" position when she is in bed or merely put into a lying position (fig. 16). The reaction of antagonists is very

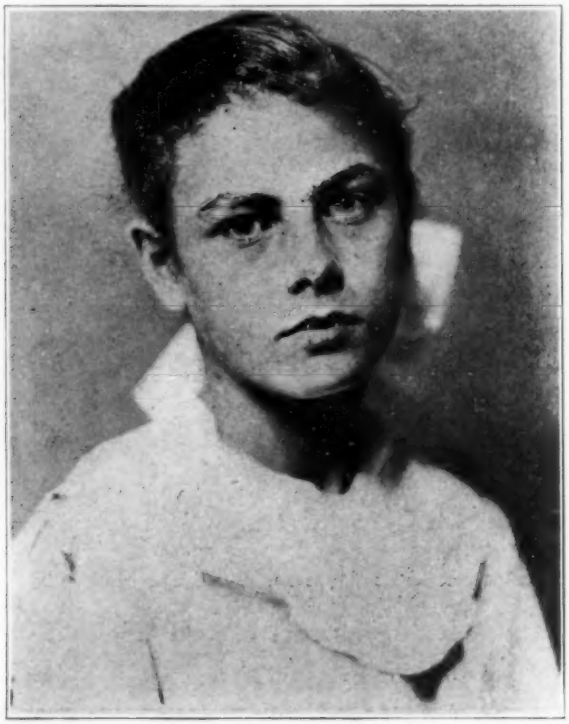

Fig. 14.—Patient in case 9, at the age of 15.

intense. The tendon reflexes are exaggerated on both sides and of low threshold, but at the same time are hypertonic, of short amplitude and abrupt. The patellar jerk shows exaggerated antagonistic contraction of the hamstring muscles. A fine tremor of the hands and of the tongue is observed. No clonus is obtained on either side. The tonic postural reflexes are exaggerated. A Babinski sign is present on both sides. Reflexes of defense are exquisitely exaggerated on both sides. The face is masklike; the left side is more immobile. Speech is so dysarthric as to be incomprehensible. The words are pronounced at the end of the expiratory phase, in a low, whispering voice. Spasmodic crying and laughing are observed. Mastication and swallowing are slow. She chokes easily; there is profuse drooling. The pupils are unequal; the left is smaller than the right; both react to light.

Fig. 15.—Same patient as in figure 14, at the age of 25. Note the flexion posture, rigidity and spasticity of the lower limbs.

Fig. 16.—The same patient as in figure 14. The flexion attitude of the lower extremities, as illustrated, is habitual.

COMMENT

Each of the cases reported represents a particular variety of clinical symptomatology and mode of evolution of deterioration in epilepsy. Cases 1, 5 and 6 are examples of early epilepsy undergoing a rapid deterioration. In case 7, the epilepsy began in early childhood (5 years), but the deterioration did not develop rapidly until the age of 18 and then in from three to four years led to deep dementia and severe cerebral flexion paraplegia, with rigidity, contracture and tendinous retractions (fig. 10). In case 4, epilepsy began not later than the age of puberty. The patient was always feebleminded. His mental and physical condition changed but little in the course of many years. When he approached the end of the fifth decade, rapid mental and physical deterioration set in, developing as a typical presenile pseudobulbar palsy. In case 3, the patient enjoyed good health up to the age of 32, when epileptic attacks began. Mental and physical deterioration developed slowly, progressed steadily and led to a typical picture of Parkinson's syndrome of paralysis agitans, not unlike the deterioration that took place in case 2, which was interesting because the mental and physical changes developed on the background of a picture of dementia praecox. Cases 8 and 9 also showed slow and steady evolution of the mental and physical condition.

The fundamental feature of the evolution of the process of deterioration which we wish to emphasize is its essentially progressive character, shown in all the cases reported and observed in many chronic epileptic patients. The progressive character of the mental and physical changes is a point of importance as it permits one to speak of these changes as a progressive deterioration of chronic epileptic patients. We provided, when possible, photographs showing the general appearance of the patients both at an earlier time and in their present condition, in order to make clear the striking changes which develop in these cases in the course of time.

The progressive mental changes in chronic epilepsy are well known, and our cases did not depart from this general rule. Emotional instability, slowness of associative processes (bradypsychia Ducosté[1]), gradual narrowing of the field of consciousness, progressing indifference and apathy (psychic rigidity) and finally more or less total dementia mark the progressive evolution of the mental deterioration. Confusional and delirious episodes are common, but systematized psychoses develop rather exceptionally in the course of epileptic deterioration. Primary feeblemindedness is present in a large majority of epileptic persons (at least in institutional material), especially in those with an onset in child-

1. Ducosté: De l'épilepsie consciente et mnésique, Thèse de Bordeaux, 1898, 1899.

hood before the age of puberty. On the background of the feeblemindedness, further mental deterioration develops.

We shall not discuss the mental aspects of deterioration. We shall proceed by studying first the clinical symptom-complex common to all the cases reported and then shall discuss the symptomatologic variants shown in individual cases.

Common Symptomatologic Pattern of Neurosomatic Deterioration in Chronic Epilepsy.—The bases of the common symptomatologic pattern are definitely progressive changes affecting the general posture and muscle tonus. A survey of the photographs shows striking and stereotyped attitudes of the head, trunk and extremities. These attitudes were observed in all of our cases, with insignificant individual variations. The head is bent on the chest (figs. 2, 3, 4, 6, 7 and 12); the trunk is inclined forward (figs. 2, 3, 7, 12 and 15); the lower extremities are more or less flexed at the knees and hips (figs. 2, 3, 4, 12 and 15); the arms are flexed at the elbows (figs. 2, 3, 4, 7 and 13); the hands and fingers are in a typical position; the wrist slightly extended (figs. 2, 3, 4, 5, 6, 7 and 13); the distal phalanges extended (fig. 1) or overextended (fig. 5); the thumb and index finger adducted, set in "pill-rolling" position (figs. 4, 6, 7 and 13); the "pill-rolling" rhythmic movements were seen in cases 3 and 4.

Studying the case histories, one finds that these postural changes developed as the first symptoms marking the actual onset of the neurologic changes of the deterioration. We shall endeavor to show that this progressive "dissolution of erectness", borrowing the expression of Kraus, develops on a background of profound modifications of muscle tonus and is to a large extent the postural expression of the muscular rigidity. The whole series of clinical phenomena testifies to the hypertonic state of the skeletal musculature in these cases. Simple inspection and palpation of the muscles gives the impression of rigor. The muscles have lost their normal softness. The ligamentous portions of the larger and more superficial muscular groups are under tension and stand out sharply under the skin (figs. 4, 7, 12, 10 and 15). More detailed examination confirms this impression and reveals the particular nature of the muscular hypertonia in our cases. Testing passive movements in the larger (proximal) and smaller (distal) joints, one meets with considerable resistance by the antagonists. This resistance is not confined to any particular group of muscles, but is shown equally by flexor and extensor groups. This resistance, on an average, is, however, more pronounced in larger segments (proximal), i.e., at the root of extremities, than in smaller segments (distal). After a passive movement is repeated several times, the resistance diminishes and in smaller segments disappears completely; in the arms, for example, performing passive

pronation and supination of the forearm, or flexion and extension of the elbow, one obtains a characteristic "cog-wheel" impression due to the alternating rhythmic contraction and slackening of antagonist muscles. Usually, this phenomenon is more pronounced on extension of the elbow and supination of the forearm. If the passive movement, as just described, is repeated several times, the cog-wheel phenomenon diminishes and may even disappear.

Testing the reaction of antagonists (Thomas,[2] Jarkowski[3]), one finds that the slightest passive displacement of a joint in one or the other direction induces an exaggerated and brisk contraction of the antagonist muscles. In our examinations of patients this test was performed on the deltoid, gluteus and triceps femoris, as only these large muscles, readily palpated, are easy to test. This phenomenon, i.e., exaggeration of the reaction of antagonists, was found to be one of the most constant symptoms in our cases.

The plastic, waxy character of muscular hypertonia in the cases studied, was well shown by two intrinsic pathologic features of the muscle tonus. First, if a segment of an extremity, say the forearm, was passively moved from its neutral rest position and then abandoned to itself, the segment tended to maintain this new position for a time and then slowly returned to the previous position; if the forearm was slightly flexed, i.e., more flexed than it was when at rest, the biceps muscle shortened a little and remained contracted for a fraction of a minute and then slowly slackened up; when the forearm was slightly extended (i.e., more extended than it was when at rest), the triceps exhibited a similar behavior. In other words, if the two insertions of a muscle were brought nearer to each other, the muscle shortened, adapting itself to the new length (adaptation tension) and maintained this length automatically by a steady contraction (fixation tension) (Foerster[4]). The muscles of the elbow, knee and ankle joints lent themselves better to the observation of this phenomena than the muscles of other segments. A slight and gentle passive displacement of a segment (forearm) produced the reaction in question more distinctly than an ample and energetic passive movement, as in the last case one easily provoked spontaneous movements on the part of the patient ("after movements"), which obscured the observation.

The second intrinsic feature of the particular muscular hypertonia shown by our patients consisted in a more or less pronounced exagger-

2. Thomas, André: Pathologie du cervelet, in Roger, Widal and Teissier: Nouveau traité de médecine, Paris, Masson et Cie, 1925, vol. 19.

3. Jarkowski, J.: La réaction des antagonistes dans le syndrome parkinsonien, Rev. neurol. **37**:613, 1921.

4. Foerster, O.: Zur Analyse und Pathophysiologie der Striären Bewegungstörungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:1, 1921.

ation of tonic postural reflexes (Foix [5]). The ankle joint and distal portion of the tibialis anticus muscle usually offered the best anatomic conditions for the observation of these reflexes. The phenomenon in question has been known for a long time as Westphal's paradoxic contraction: If the ankle is flexed dorsally and rotated slightly inward, then promptly abandoned to itself, the tendon of the tibialis anticus contracts under the skin and remains so for a while; then it gradually relaxes, allowing the foot to return to its neutral position (Foix and Thévenard [6]). In our observation, the exaggeration of tonic postural reflexes was very common and well expressed. Of course, the exaggeration of tonic postural reflexes can be regarded as a case of fixation tension observed in the tibialis anticus muscle.

Taking into consideration the particular properties of muscular hypertonia, as shown in our cases, namely, plastic resistance of muscles to passive movements, exaggeration of reaction of antagonists, adaptation and fixation tension of muscles, exaggeration of tonic postural reflexes, we can say that this hypertonia is of a particular nature and different from the spastic condition of muscles observed in lesions confined to the pyramidal system. The cases uncomplicated with symptoms of the pyramidal series showed all these features of rigidity particularly well (cases 1, 2 and 3), and more so on the side of greater hypertonia. The progressive muscular rigidity developing in the course of deterioration and associated with characteristic modifications of normal tonic and postural reactions, as just described, constitutes the background of the clinical picture presented by these cases and influences many of the other characteristic symptoms. With the progress of rigidity, the general hypokinesis increases, voluntary movements become slow and monotonous. When the patient is standing or when he attempts to walk, more or less distinct propulsion (cases 3, 4, 5 and 9) or retropulsion (cases 6 and 8) is present. Associated movements of the arms are absent or greatly reduced. The steps become short and unequal, because the rigidity is often unequally developed on the two sides, and the more rigid leg makes shorter steps; the gait is trotting ("à petit pas"), particularly in cases with the more developed pseudobulbar features (cases 4, 5 and 6). The facies becomes masklike, rigid and inexpressive (figs. 3, 4, 7, 10 and 13). The facial rigidity sometimes predominates on one side and this is particularly evident when the patient is smiling (fig. 15). The mouth is partially open and there is more or less profuse drooling in most cases as these patients do not swallow the saliva that accumulates in the mouth; the tongue can be only partially protruded. The speech "en plateau," so characteristic in chronic epilepsy, is the

5. Foix, C.: Réflexes toniques de posture, Rev. neurol. **2**:840, 1130, 1921.

6. Foix, C., and Thévenard, A.: Les réflexes de posture, Rev. neurol. **39**:449, 1923.

first stage in the evolution of disturbance of phonation and word articulation. The speech becomes thick and slow; the voice becomes more monotonous. Words are poorly articulated (dysarthria) and pronounced in a low voice (hypophonesis); the patient answers questions in a monosyllabic manner, the words coming at the end of expiration. Often, palilalic repetition of the same syllables or words is observed. The speech defect becomes complete. The patient appears to be mute[7] (case 7). The pill-rolling movements in the fingers have been mentioned. Tremor of the head (cases 3 and 4), and tremors of the hands (cases 1, 2, 3, 5 and 6) are common. The intensity of the tremor is variable; the tremor is at times coarse so that in some cases it can be registered on a photographic plate (figs. 2 and 5). The tremor is usually rhythmic, persisting at rest, and not increased by voluntary movements (static tremor). Tremor of the fingers is observed in all cases and is of a finer, oscillating type. Tremor of the tongue is almost invariably present, and occasionally tremor of the lips is observed.

The tendon reflexes undergo qualitative modifications which we consider to be highly characteristic of muscular rigidity. The tendon reflexes acquire a particular hypertonic character. Usually, the patellar response exhibits these qualitative modifications best. The tendon reflexes become, on the whole, exaggerated; that is, the threshold of effective stimulus becomes relatively lower while the intensity of response is higher than in the average normal response. In spite of this, the amplitude of the jerk, i. e., the excursion of the stimulated segment, becomes reduced and disproportionally short. In the patellar jerk, the reflex extension of the leg on the thigh is abruptly blocked by intense antagonistic contraction of the hamstring muscles, an example of the exaggerated reactions of antagonists. In the more advanced cases (cases 2, 8 and 9), when eliciting the patellar jerk, the leg becomes immobilized at the end of a short excursion. By repeated mechanical stimuli applied to the patellar tendon one obtains successive and abrupt extension jerks, the leg remaining immobilized each time at a more open angle to the thigh until finally it becomes completely extended. The leg remains in this position for a fraction of a minute and then gradually returns to the neutral position. This immobilization of the leg at the end of each short reflex excursion is produced by simultaneous tension of both extensors and flexors of the knee; an example of the described fixation tension, or of shortening (quadriceps femoris) and lengthening (triceps femoris) reactions.

Together with the increase of general hypokinesis and exaggeration of muscular tonus, a progressive lack of reactive movements is observed.

7. Muteness is many times only apparent, for under the stimulus of an emotion, particularly anger, they can talk. The nurses often say, "No, they cannot talk but they can swear all right."

Both the emotional and motor reactions of the patients to unpleasant stimuli become reduced and sometimes completely inhibited. In eliciting reflexes of defense in the lower extremities, according to usual technics (Babinski,[8] Marie, Foix[9]), one does not obtain any, or only a very slight, response. Thus, especially in cases that are not complicated with pyramidal or pseudobulbar features, the reflexes of defense are diminished or abolished (cases 1, 2 and 3). Also, certain skin reflexes become rigid, dull and less responsive to the average stimuli; for example, plantar reflexes, as was found in the cases just referred to.

The clinical features described are the conspicuous elements of a typical akinetohypertonic syndrome which is the most constant, basic clinical expression of progressive neurologic changes shown in a greater or lesser degree by the whole series of recorded cases. We shall see later that certain intrinsic features of this akinetohypertonic symptom-complex are detected in a neurologic survey of a large number of epileptic patients. This symptom-complex, in our opinion, constitutes a general clinical pattern of neurosomatic deterioration of chronic epileptic patients.

In cases 1, 2 and 3, the akinetohypertonic syndrome is found in a clearcut and uncomplicated form. In case 1 the characteristic picture developed following a severe status epilepticus, though progressive hypokinesis and rigidity were evident to some extent before the patient developed status, in which he died. The flexion attitude of the body and extremities, tremor of the fingers, severe generalized rigidity, exaggerated reaction of antagonists, exaggerated tonic postural reflexes, characteristic modification of tendon reflexes, abolished reaction to painful stimuli, absence of the reflexes of defense, masklike, inexpressive facies, drooling, monotonous, economically retailed speech, general hypokinesis, lack of associated movements, all developed after recovery from status, were so striking as to attract immediate attention. However, detailed examination did not reveal in this case any of the commonly accepted clinical symptoms of the pyramidal series: no clonus of the foot; plantar reflexes sluggish but with the response invariably flexor in type; no spastic contracture; no motor paralysis in the proper sense of the word; all voluntary movements extremely slow and rigid but preserved, and without noticeable and elective diminution of muscular force.

In case 2, exactly the same clinical picture was found. In this case the akinetohypertonic symptom-complex, with characteristic postural changes, developed gradually in the course of from ten to fifteen years.

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8. Babinski, J.: Réflexes de défense, Rev. neurol. **38**:1049, 1922; Brain **45**: 149, 1922.

9. Foix, C.: L'automatism médullaire, in Questions neurologiques d'actualité, Paris, Masson et Cie, 1929.

Here again, no evidence of pyramidal lesions was present. Muscular rigidity was generalized without contracture of elective groups of muscles; there was no clonus or Babinski sign. Muscular force was well preserved.

Case 3 was particularly rich in interesting clinical suggestions. The patient was a healthy man up to the age of 32. Without evidence of syphilis, encephalitis, alcoholism or cerebral injury, he then began to have epileptic convulsions and, ten or fifteen years later, developed a steadily progressing picture of typical paralysis agitans. The sluggishness of the left patellar reflex and abolition of the left achilles reflex, which had appeared in the course of the last year or two, at first compelled us to think of a possible cerebral syphilis with the development of a mild Wilson-Cobb [10] syndrome-mesencephalitis syphilitica. However, there was no other evidence of cerebral syphilis. One cannot give much weight to the temporary sluggishness of light reflex found on a few occasions, particularly when one deals with an epileptic person (Westphal [11]). There was no Romberg sign. Vibration sense and position sense were preserved in both lower extremities. Repeated Wassermann tests with the blood and the spinal fluid were negative. The spinal fluid gave normal results as to the protein content and was free from cells. Cerebral arteriosclerosis, as the pathologic basis in this case, seems to be much more plausible, yet the patient never showed an increased blood pressure and the urine was normal. Whatever might be the exact cause and nature of the pathologic process underlying the epileptic convulsions and subsequent neurologic changes observed, it is obvious that the present clinical picture is extremely like the clinical picture developed in the course of chronic epilepsy in cases of a quite different type and etiology (cases 1 and 2). In six other observations (cases 4 to 9), though important symptoms of quite different type were found the same general symptomatologic pattern was present, showing the same clinical evolution as in cases 1, 2 and 3; namely, epilepsy, impairment of mental faculties, gradual postural changes, progressive muscular rigidity, general hypokinesis, tremor and masklike facies, also the characteristic changes of phonation, speech and hypersalivation.

It is of interest to note in connection with this akinetohypertonic symptom-complex of chronic epilepsy that the characteristic clinical picture was described not infrequently in the case reports that were found in the casuistical survey of the old and the new literature on epilepsy and on related conditions. It is impossible to review extensively

10. Wilson, S. A. K., and Cobb, S.: Mesencephalitis Syphilitica, J. Neurol. & Psychopath. **5**:44, 1924.

11. Westphal, A.: Ueber eigenartige Einschlusse in den Ganglienzellen (Corpora Amylacea) bei einem Fall vom Myoklonus-Epilepsie, Arch. f. Psychiat. **60**: 769, 1919.

the subject here, but we will refer to a few particularly suggestive observations. Unverricht [12] and Lundborg,[13] in several publications, described a special clinical form of chronic epilepsy associated with myoclonus, both frequently of familial and hereditary occurrence. This particular type of epilepsy has been recorded since as the Unverricht-Lundborg syndrome. In many cases of this type the deterioration sets in and progresses rapidly. In its clinical evolution, three periods, usually overlapping each other, can be discriminated (Lundborg). The disease begins with epileptic convulsions, usually nocturnal, (first or "epileptic stage"); later, myoclonus becomes associated with the epileptic attacks (second stage, "epilepto-myoclonic"); finally, the third stage ("terminal or marantic stage") develops, which interests us here in particular. The epileptic attacks in this period become less frequent and often completely disappear; the myoclonus continues; at the same time the patients gradually develop a condition much like paralysis agitans, with generalized rigidity, flexion attitude of the body and extremities, masklike face, tremor and hypersalivation. The analogy with the parkinsonian syndrome was pointed out by both original authors and is evident in their case reports as well as in those of many subsequent writers (Crouzon [14]).

From our observations as recorded and from the clinical survey of a much larger material, it appears that this particular picture, developing in the advanced degrees of deterioration, is not specific for myoclonus-epilepsy alone, but is found in chronic epileptics without myoclonus as well. The peculiar fact of the diminution and even disappearance of epileptic attacks in the terminal stage of myoclonus epilepsy of the Unverricht-Lundborg type is not alone found true for the cases of myoclonus epilepsy, but holds good for many cases of chronic epilepsy in which a more or less advanced degree of progressive muscular rigidity and other symptoms of the akinetohypertonic pattern of deterioration develop. The intervals between isolated attacks become longer. The average number of convulsions in any given period of time might even increase because the seizures in some cases tend to run in series and develop into a status, but during the long intervals between the series or status no isolated convulsions occur. In case 1, during ten days between two status periods, while rigidity was at its highest, the patient had no convulsions. The diminution of attacks seems to bear particularly on the frequency of grand mal attacks (complete seizures). The convulsive paroxysms change their clinical expres-

12. Unverricht: Ueber familiare Myoklonie, Deutsche Ztschr. f. Nervenh., 1895.

13. Lundborg: Die Progressive Myoklonus-Epilepsie, Upsala, 1903.

14. Crouzon, O.: Myoclonie familiale, in Traité de pathologie médicale et de thérapeutique appliquée, Neurologie, Paris, A. Maloine et fils, 1924, vol. 2, p. 400.

sion, become milder, less dramatic and of shorter duration and the clonic component is less pronounced (cases 3, 4 and 6). However, it must be kept in mind that one can speak of a general tendency of reduction and eventual disappearance of convulsions without inferring that the convulsive capacity of the patient is actually lost. In some cases, after grand mal seizures have subsided for several years, the patient has had a severe epileptic attack or has developed status, which has often resulted in death.

The case reports of the akinetohypertonic syndrome developing in chronic epilepsy and having a close analogy with the syndrome of Parkinson has become more frequent in recent literature than heretofore. In 1925, Urechia,[15] in collaboration with Elekes and Mihalescu, published the observation of a chronic epileptic patient who a few years before death developed a typical picture of paralysis agitans. Epileptic attacks ceased completely.

In 1926, Toulouse, Marchand, Bauer and Male [16] described two cases of chronic epilepsy with mental enfeeblement and the progressive development of a parkinsonian syndrome. One of us,[17] in a brief preliminary communication made before the Boston Society of Psychiatry and Neurology, in October, 1927, discussed cases 3 and 6 of the present paper in connection with two other cases of postencephalitic epilepsy, and pointed out the frequency of symptoms of parkinsonism in deteriorated epileptic patients and the diminution or complete disappearance of epileptic seizures in the cases showing advanced rigidity. In 1928, Courtois [18] in an interesting thesis, made exactly the same observations in a series of chronic epileptic patients and proposed to individualize the whole symptom-complex under the name of "syndrome comitio-parkinsonien."

The akinetohypertonic syndrome developing in chronic epilepsy appears, therefore, to be a fact observed by several authors independently of each other.

No doubt, the definition "syndrome comitio-parkinsonien" proposed by Courtois is well chosen with regard to a group of cases such as our case 3, and also cases 1 and 2 reported by one of us as already cited. However, when attempting to study these progressive neurologic changes on a large clinical material, one finds that such definition becomes too narrow and also, perhaps, too specific, fitting only a rela-

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15. Urechia and Mihalescu: Épilepsie et parkinsonisme, Rev. neurol. **2**:99, 1927.

16. Toulouse, Marchand, Bauer and Male: Encéphale **24**:808, 1926.

17. Yakovlev, P.: Epilepsy and Parkinsonism, New England J. Med. **198**:629, 1928; Arch. Neurol. **19**:555 (March) 1928.

18. Courtois, A.: Syndrome comitio-parkinsonien: Étude anatomo-clinique, Thèse de Paris, 1928.

tively small group of cases. Studying the neurologic changes developing in the course of deterioration as a general clinical phenomenon, one finds that the akinetohypertonic symptom-complex ("syndrome comitio-parkinsonien," of Courtois), though presenting sometimes a very close analogy with the classic parkinsonian syndrome, must not be identified altogether with the latter. The progressive mental enfeeblement and important symptomatologic variants developing on the background of the akinetohypertonic pattern syndrome, generally speaking, are foreign to the classic syndrome of Parkinson while they play a conspicuous rôle in the further clinical evolution and in the symptomatology of the progressive neurosomatic deterioration of chronic epilepsy.

Symptomatologic Variants of Neurosomatic Deterioration in Chronic Epilepsy.—The variants in question can be summarized under three groups of symptoms: (1) progressively developing and eventually bilateral symptoms of the pyramidal series, with spasticity predominating in the lower extremities (Cases 4, 5, 6, 8 and 9); (2) progressively developing symptoms of the pseudobulbar type, with exaggeration of the reflexes of defense and a tendency to flexion contracture, predominating in the lower extremities (cases 4, 5, 6, 7 and 9); (3) ultimate flexion paraplegia of cerebral type with tendinous retractions and advanced dementia (case 7).

In cases 1, 2 and 3, there was an akinetohypertonic syndrome uncomplicated with symptoms of the pyramidal series. The outstanding features of these cases were generalized muscular rigidity of plastic type, exaggeration of tonic postural reflexes, diminution or the actual abolition of the reflexes of defense and of general reactive movements (lack of emotional reaction on painful stimuli); there were no contractures and no clonus of the foot; the plantar reflexes were of flexor type. In the other six cases (cases 4, 5, 6, 7, 8 and 9) the clinical picture is different.

The most striking modification of the akinetohypertonic pattern in these cases consists in an exaggeration of the reflexes of defense (cases 4, 5, 6, 7 and 9). Slight pinching of the skin of the lower extremities (ankle) induced an intense and sustained spasm of the flexors with retraction of the stimulated lower extremity and dorsiflexion of the foot. Sometimes, a unilateral stimulus produced a similar reaction in the opposite extremity, usually delayed and less complete. The motor response in the lower extremities was usually accompanied by a pronounced emotional reaction (deep inspiration, flushing of the face and crying), which lasted not longer than the motor reaction in the lower extremities.

Another feature of these cases was the presence of definitite symptoms of the pyramidal series. Except in case 7 (which will be considered later), in all other cases (4, 5, 6, 8 and 9), a bilateral extensor response was present; clonus was found in some cases (in case 4 in the right

foot; in case 6 on both sides). The character of the muscular rigidity in these cases, as compared to uncomplicated cases (cases 1, 2 and 3) showed some modifications, particularly with regard to the lower extremities. The muscular hypertonia was more elective and predominated in the flexors of the hip, knee and ankle. On passive extension of the lower extremities, a contracture of a spastic character was prominent (cases 5, 6, 7, 8 and 9). The reaction of antagonists was found exaggerated, particularly with regard to the flexors of the lower extremities. On the contrary, the tonic postural reflexes in some cases became diminished (cases 4 and 6), though in other cases they were not noticeably modified. On an average, the tendon reflexes were of comparatively lower threshold, though they always maintained their hypertonic character (short amplitude, fixation of the knee in extension phase and exaggerated hamstring contraction). In some cases they became diminished and even abolished (case 7). In the cases complicated with bilateral pyramidal symptoms, as already enumerated, together with a more advanced dementia were pronounced and strikingly constant and characteristic symptoms of the pseudobulbar type: disturbance of speech (dysarthria), of deglutition (dysphagia), spasmodic emotional reactions (spasmodic crying and laughing), drooping head and lower jaw and short-stepping gait (cases 4 to 9).

Together with the progress of mental deterioration, the patients showed an increasing tendency to acquire spontaneously, as well as under the influence of external stimulation, a highly characteristic, stereotyped, "clasp-knife" posture when in a recumbent position. The whole body doubled up, the lower extremities were drawn up on the abdomen, the legs flexed on the thighs, and the feet scissor-crossed (figs. 8, 10, 13 and 16). The propensity to acquire this attitude when in bed was shown in varying degree in all cases. Cases 6, 7, 8 and 9 showed this feature particularly well. Some patients become, or tend to become, permanently confined to bed (cases 6, 7, 8 and 9). With an increase of flexion contracture and "clasp-knife" posture, the passive extension of the lower extremities becomes more and more limited; unassisted walking, and even standing, becomes difficult (cases 6, 8 and 9) and sometimes impossible (case 7). It must be stated clearly that voluntary movements in the lower extremities, though greatly reduced in force, in range and in variety, remain possible until tendinous retractions set in. This condition was exemplified in case 7. The doubled up, "clasp-knife" attitude of this patient became, so to say, definitely fixed by severe tendinous retractions (fig. 10). Developing first in the distal joints, the tendinous retractions were more pronounced in the foot and knee flexors than in the hip flexors. With the progress of the flexion contracture and tendinous retractions, the voluntary move-

ments in the lower extremities became abolished. Trophic changes of the muscles and joints set in. The muscles underwent general atrophy; the knee joints became deformed, and the femoral bone of the left leg was detached from the cartilage. One can see in figure 10 the severe flexion contraction and tendinous retraction of the knee, foot and toes. A plantar response could not be obtained. The reflex of defense was evident in flexion of the thigh on the abdomen induced by stimulation of the skin of the legs. Passive movements were impossible. On the contrary, in the upper extremities, though flexion contracture was evident (fig. 10), no tendinous retractions were present; voluntary movements were preserved to a considerable extent.

In the presence of this symptom-complex one could speak of true paraplegia of flexion type. This type of paraplegia is the ultimate stage of neurosomatic deterioration. Very few patients reach this stage, but the condition is relatively common in an institution for epileptic patients. We could offer a whole series of photographs absolutely identical with figure 10. Three of them were given in the paper [17] by one of us already quoted. The flexion paraplegia, as shown in case 7 and in many other examples in the hospital, must be differentiated from the spinal flexion paraplegias, as observed, for example, in cases of slow compression of the spinal cord, in spite of the apparent analogies between them (Alajouanine [19]). Taking case 7 as an example, one can see that in this case flexion contracture, with ultimate fixation of the lower extremities in the "clasp-knife" posture, took place following a particular and typical clinical evolution: epilepsy, progressive mental enfeeblement, generalized rigidity, bilateral pyramidal symptoms, symptoms of pseudobulbar type, exaggeration of reflexes of defense and, finally, flexion contracture of the lower extremities with tendinous retraction. The symptomatology presented by this case shows important differences as compared to the symptomatology of spinal flexion paraplegia. In the latter there are usually pronounced sensory disturbances (anesthesia) of segmental character, early disturbances of sphincter function, with retention and involuntary automatic micturition and defecation, prompt development of bed sores and early loss of voluntary motion in the lower extremities. On the contrary, in flexion paraplegia, such as we describe in chronic epilepsy, voluntary motion, though gradually reduced, remains possible for a long time until tendinous retractions set in, so that for a long time one can speak merely of the "flexion attitude" (cases 5, 6, 7 and 9) and only at an ultimate time of a true flexion paraplegia of cerebral type. Bed sores in these cases do not develop as easily; if

19. Alajouanine, T.: Sur un type de paraplégie en flexion d'origine cérébral avec exagération de l'automatisme médullaire, Arch. franç. de pathol. gén. et expér. de anat. pathol., 1923, no. 5.

developed, they heal more rapidly than in cases of spinal paraplegia, suggesting greater integrity of the spinal trophic centers in the first type than in the latter. The patients are untidy as a result of the dementia, but they do not show sphincter disturbances of a spinal type, with retention of urine and permanent incontinence of urine and feces. They do not show anesthesia in the lower part of the body; on the contrary, they show an explosive emotional reaction to stimuli; the lower extremeties are, as a rule, hyperalgesic. No definite segmental level for the reflexes of defense can be established.

The flexion paraplegia, as found in case 7 and in many other similar examples, is unquestionably of cerebral origin, as is the whole symptomatology of the neurosomatic deterioration of chronic epileptic patients. Further discussion of this particular variety of flexion paraplegia of cerebral type is beyond the scope of the present paper.

In this series of observations illustrating various degrees of neurosomatic deterioration, one can discriminate, more or less schematically, three phases in the clinical evolution: (1) the phase of more or less well expressed akinetohypertonic syndrome (epileptic parkinsonism) which may remain for a long time without association with symptoms of pyramidal type; (2) the phase of associated and eventually bilateral pyramidal symptoms of cerebral origin, with frequent development of the pseudobulbar phenomena; (3) the phase of advanced dementia, with flexion contracture of the lower extremities and tendinous retractions.

Careful study of the early histories in our cases and of the mode of evolution of the progressive neurologic changes, as described, compels us to conclude that these phases do not represent independent clinical syndromes due to some accidental lesions or intercurrent diseases, but are the clinical expression of progressive neurosomatic deterioration developing in the course of a more or less long-standing chronic epilepsy. It appears as if a common pathologic process, underlying both the epilepsy and the subsequent deterioration, in the course of time was becoming more destructive and more diffuse, progressively involving cerebral functions hitherto not impaired.

In case 6, particularly illustrative from this standpoint, the neurologic changes started with typical akinetohypertonic symptoms. Later, a suggestion of an extensor response was noted in the left foot at the same time that reflexes of defense became exaggerated, with a hyperalgesic emotional reaction. Within about a year, a bilateral Babinski sign developed; reflexes of defense became exquisitely exaggerated; flexion contracture in the lower extremities became more pronounced; clonus appeared on both sides, and the postural reflexes diminished. At the same time, pseudobulbar symptoms came out clearly, with dysarthria,

dysphagia and spasmodic laughing and crying. Unassisted standing and walking gradually became difficult; the patient became confined to bed, showing a characteristic "clasp-knife" posture of the lower extremities.

In case 7 we met with exactly the same order of evolution of different symptomatologic components of progressive neurosomatic deterioration; however, the whole process developed at a later age and reached a more advanced stage of complete dementia, with fully developed cerebral flexion paraplegia and severe tendinous retractions in the lower extremities.

Of course, the various symptomatologic components, i.e., akinetohypertonic, pyramidal, pseudobulbar and dementia, do not necessarily follow the same order of evolution in every case; often they overlap each other in the time of onset and in further progress, so that one cannot speak of sharply successive phases in the clinical progress of deterioration. If, on an average, the akinetohypertonic symptoms are first to set in and usually dominate the clinical picture, in the further evolution of the deterioration (case 8), however, it is not uncommon that pyramidal symptoms develop before other neurologic changes become fully evident. In case 9 we have a good example of such an evolution. Eight or nine years after the onset of epilepsy, the first neurologic sign noted was a suggestion of a Babinski sign in the left foot (at the time of the second admission). Two and a half years later (at the third admission), definite extensor response and bilateral foot clonus were noted. Only after this third admission did the akinetohypertonic symptoms become evident. The Babinski sign became bilateral. Rigidity continued to increase; the tonic postural reflexes became exaggerated, and clonus of the foot ceased to be elicitable; reflexes of defense became distinctly exaggerated, and eventually pseudobulbar symptoms (dysphonia, dysarthria and dysphagia) set in together with advanced dementia. In case 4 all the components of the patient's existing neurologic symptom-complex—(1) progressive rigidity and tremor, (2) bilateral pyramidal symptoms, (3) disturbance of speech, mastication and swallowing—developed gradually; one was not able to say whether akinetohypertonic or pyramidal and pseudobulbar symptoms set in first. The deterioration set in and progressed as a typical syndrome of pseudobulbar palsy, with the pronounced extrapyramidal symptomatology described by Foerster, Lhermitte [20] and others. It is not without interest to note that the patient developed a pseudobulbar syndrome at the age of 45, without previous apoplectiform attacks and without showing at any time increased blood pressure or cardiorenal disturbances.

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20. Lhermitte, J.: Les syndromes striés du viéllard, Rev. neurol. **38**:406, 1922.

Residual Syndromes (Sequelae) of the Primary Cerebral Lesion and the Symptom-Complex of Progressive Neurosomatic Deterioration.—The essentially progressive syndrome of neurosomatic deterioration, developing in some cases many years after the onset of epilepsy (cases 4, 7 and 9), must not be confused with nonprogressive and often regressive residual syndromes or sequelae of a primary cerebral lesion, such as are found commonly in chronic epileptic patients, especially among the inmates of institutions. Cases 5 and 8 gave good examples of the syndromes of two respective clinical types associated in one symptom-complex. In case 5, the patient, at the age of 5, had an illness not definitely described, but probably of a meningo-encephalitic nature. She then had the first epileptic convulsion; following this the left side was paralyzed. The paralysis cleared up within a short time. However, on admission, three years later, a neurologic examination showed a latent left-sided infantile hemiplegia. In the course of the following two and a half years, deterioration made distinct progress; rigidity was noted on both sides of the body, being more pronounced on the right, nonhemiplegic side. Later, pyramidal symptoms (extensor response) appeared on the right side also. At the same time, symptoms of a pseudobulbar type set in. The symptoms of a latent pyramidal hemiplegia on the left side remained unchanged, except that rigidity took the place of a relative hypotonia and the involuntary movements became less evident.

In case 8, the clinical history is even more illustrative, as between the onset of the syndrome of infantile hemiplegia with epilepsy and the onset of the first progressive neurologic changes not less than fifteen years elapsed. Again there was a mild but well developed infantile hemiplegia with spastic contracture of the flexors and pronators of the upper extremity and a paralytic clubfoot on the left. On admission, the patient, then 18, showed all the pyramidal symptoms on the left side associated with hemiplegia. About ten or twelve years later, deterioration began to make definite progress; mental impairment was accompanied by characteristic neurosomatic changes: rigidity; a flexion posture of the head, trunk and extremities; gait and standing became difficult; flexion contracture developed in both lower extremities; definite pseudobulbar symptoms set in. At the present time the patient shows extensor response on both sides, extreme generalized rigidity with a cog-wheel sign in the right arm; tonic postural reflexes, though less pronounced on the side of the hemiplegia, became exaggerated on both sides while foot clonus disappeared, a fact which would appear paradoxic if one did not admit the definite changes in the sphere of muscle tonus innervation which developed in the course of deterioration. Severe generalized rigidity at the present time dominates the clinical picture in this case. In spite of all these neurologic changes, the infantile hemiplegia has remained unchanged as to the degree of paralysis of voluntary

movements, severity of spastic contracture or diminishing of the muscular power in the affected extremities.

In cases 1, 7 and 9 we have a negative counterpart of cases 5 and 8. In these three cases there is no doubt that the primary cerebral lesion was the direct causative factor of the epilepsy. In case 1, the patient, when 6, had measles and the first epileptic convulsion—a complication of measles with encephalitis of toxic infectious nature is highly probable. In case 7, the patient, already constitutionally predisposed (talked and walked late), when 5 had a severe head injury, was ill several days, and then had his first epileptic convulsion. In case 9, the patient, when 6 had a meningo-encephalitic attack (medical information) and began to have epileptic convulsions. However, in spite of a definite history of a primary cerebral lesion, none of these cases showed residual neurologic signs at the time of admission to the hospital. Notwithstanding this, definite neurologic changes developed in all three cases in the course of the subsequent deterioration, even as late as nine years after the occurrence of the primary cerebral lesion with the onset of epilepsy in case 9, and not less than ten years after such a lesion with the onset of epilepsy in case 7.

In cases 2 and 6, the primary cerebral lesion was not evident either from the history or from the neurologic examination at the time of admission. In the further clinical evolution, both patients developed definite neurologic changes.

In our records of the neurologic survey of chronic epileptic patients, now consisting of over 500 cases, such examples are common. From these observations it appears that the neurologic symptoms eventually developing in the course of more or less long-standing epilepsy, which we consider as a clinical expression of neurosomatic deterioration, are different in nature and are independent in their clinical evolution from the residual syndromes (sequelae) of the primary cerebral lesion so often found in chronic epilepsy.

Akinetohypertonic and Pyramidal Syndromes as Shown in Cases of Advanced Neurosomatic Deterioration.—We have already pointed out and sufficiently emphasized that in the cases presenting a well developed akinetohypertonic symptom-complex, uncomplicated with symptoms of the pyramidal series, there was a great deficiency of reactive movements (cases 1, 2 and 3). Reflexes of defense were absent (case 1). Pinching the skin of the back of the ankle in these cases did not produce any protective movement on the part of the stimulated extremity. Also, emotionally the patient remained absolutely indifferent, though the stimulus applied surely was above the threshold of pain tolerance of a normal person. In these cases there was no true anesthesia; the patients adequately perceived and discriminated pinching from pin-pricks, and a

glass tube of hot water from an ice block. The patient in case 1, when asked, stated that "it is sore," and yet not the slightest spontaneous motor or emotional reaction betrayed the pain he consciously experienced when the skin of the leg or thigh was pinched. In all cases the plantar response, though flexor in type, was extremely dull and sluggish.

The inhibition of the motor protective reaction (abolishing of reflexes of defense), the emotional indifference to painful stimuli (emotional hypalgesia or analgesia) and the sluggishness of plantar response have been observed by various authors in certain so-called extrapyramidal rigidity syndromes (parkinsonian rigidity—arteriosclerotic rigidity) and especially emphasized by Foerster.[4] These features are very common in chronic epilepsy and belong among the early symptoms of neurosomatic deterioration.

If one considers from the standpoint of these reactions the cases presenting, on the background of rigidity, the well developed symptoms of the pyramidal series (plantar extensor response and spastic contractures), one meets with a striking contrast (cases 4, 5, 6 and 9). Even moderately painful stimulation of the skin of the lower extremities (back of the ankle) induces promptly an intense and widespread defense reaction in which two components should be discriminated: one, the local motor reaction, and the other the general emotional reaction. Slight pinching of the back of the ankle induces a spasm in the stimulated lower extremity, dorsiflexion of the ankle (sometimes extension of the toe) and flexion withdrawal of the leg (sometimes of both legs)—a typical exaggerated reflex of defense (Babinski[8]). At the same time, a general emotional reaction of the patient is observed: flushing of the face, grimacing, deep inspiration and spasmodic crying. This "emotional hyperalgesia," contrasted with the "emotional analgesia" in cases uncomplicated with the pyramidal symptoms, recalls, trait by trait, the "surréflectivité hyperalgèsique" described by Babinski and Jarkowski[21] in certain cases of cerebral hemiplegia and in cases of the high Brown-Séquard syndrome. It is interesting to mention that in our cases this spasmodic emotional and motor reaction lasted not longer than the stimulus; with the removal of the latter it rapidly disappeared, thus enhancing its largely automatic reflex nature.

The behavior of the tonic postural reflexes in cases of uncomplicated akinetohypertonic syndrome and in cases in which this syndrome was complicated with the symptoms of the pyramidal series constitute another interesting contrast. In cases 1, 2 and 3, the tonic postural reflexes (phenomenon of the tibialis anticus) were highly exaggerated (delayed phase of postural decontraction), and more so on the side of the greater rigidity. On the contrary, in the cases presenting the

21. Babinski, J., and Jarkowski, J.: De la surréflectivité hyperalgésique, Rev. neurol. **37**:433, 1921.

association of pyramidal symptoms (cases 4, 5 and 6) the tonic postural reflexes were diminished or became diminished with the onset of an extensor response (case 6).

The akinetohypertonic and the pyramidal components of the clinical picture in these cases exhibit a sort of reciprocal antagonism, the rigidity counteracting the amplitude of the reactive movements and intensifying the tonic postural reflexes, while the pyramidal spasticity exaggerates the reflexes of defense and the spasmodic emotional reaction but at the same time diminishing the tonic postural reflexes. In case 6, the exaggeration of reflexes of defense with spasmodic emotional reaction and diminishing of the tonic postural reflexes coincided with the onset of bilateral extensor response and appearance of foot clonus. In case 4, tonic postural reflexes, reaction of antagonists, were relatively better maintained on the left and more rigid side of the body, while the reflexes of defense, emotional hyperalgesia and diminution of tonic postural reflex, predominated on the right side of the body; that is, on the side on which spastic contracture, exaggeration of tendon reflexes, extensor response and foot clonus were more pronounced. Also, in case 5 the muscular rigidity with its respective intrinsic symptoms was more distinct on the right nonhemiplegic side, in spite of the presence of a bilateral extensor response.

The antagonism between akinetohypertonic and pyramidal symptoms can result in the predominance of one or the other of these two components. We have seen that in case 6 symptoms of the akinetohypertonic component developed first and became later modified, masked to a certain extent by the symptoms of the pyramidal series. In case 9, on the contrary, at first pyramidal symptoms were found; there was an extensor response and bilateral foot clonus; later, when rigidity progressed, tonic postural reflexes became exaggerated and clonus disappeared. In advanced cases the association of symptoms of the akinetohypertonic type and of the pyramidal type can result in a most intricate symptomatologic blend, as shown for example in case 8; the akinetohypertonic syndrome with its basic feature, severe generalized rigidity, was particularly well developed in this case, and in spite of a bilateral extensor response and spastic contractures, shown in the lower extremities, the reflexes of defense were abolished and emotional reaction to painful stimuli was absent; tonic postural reflexes were much exaggerated on both sides and foot clonus, recorded in the earlier observations on the left hemiplegic side, was no longer elicitable. These last two cases (8 and 9) illustrate again a general rule that the tonic postural reflexes and foot clonus are clinically opposed phenomena. This point was strongly emphasized by Delmas-Marsalet [22] in his studies of

22. Delmas-Marsalet, P.: Les réflexes de posture élémentaires, Paris, Masson et Cie, 1927.

postural reflexes. This author has shown, for example, that inhibiting the tonic postural reflexes by hypodermic injections of scopolamine bromide, in doses of 1.5 mg. in a solution of 1 : 2,000, in some cases that presented a parkinsonian syndrome, while the muscular rigidity disappears and the tonic postural reflexes become abolished the symptoms of the pyramidal series become elicitable. This author believed that in such cases a latent pyramidal lesion was present but was masked by the rigidity. His contention is that the scopolamine test can be used as a means for the detection of such latent pyramidal lesions. Similar views have been expressed also by Walshe.[23]

We have repeated the same experiment on twenty-five young epileptic patients and ten normal persons of both sexes, all between the ages of 20 and 30 years. All were carefully examined before the injection of scopolamine and then fifteen minutes, half an hour, one, two and three hours after giving a dose of $\frac{1}{50}$ grain (1.3 mg.). In from fifteen to thirty minutes after the injection, in all persons, epileptic and normal, muscular hypotonia developed. The tonic postural reflexes were abolished while gross pyramidal symptoms became elicitable (bilateral extensor response, bilateral foot clonus, Oppenheim sign, exaggeration of tendon reflexes). These symptoms persisted on an average for two hours after the injection and then disappeared. Continuing the experiment with smaller doses of the drug ($\frac{1}{75}$, $\frac{1}{100}$ and $\frac{1}{200}$ grain [0.83, 0.6 and 0.3 mg.]), we found that while $\frac{1}{100}$ and even $\frac{1}{200}$ grain was sufficient to provoke pyramidal symptoms in most epileptic patients, in normal persons a dose of $\frac{1}{75}$ grain gave inconstant results and after a dose of $\frac{1}{150}$ grains (0.4 mg.) no one developed pyramidal symptoms. Thus, according to our results, the difference between normal and pathologic cases was merely quantitative, a higher dose of the drug being required to obtain the same effect in normal as compared with epileptic persons. These experiments confirm the observations of Delmas-Marsalet as to the emergence of pyramidal symptoms and especially the appearance of foot clonus when the tonic postural reflexes are inhibited by disease of the pyramidal system or by the specific effect on these reflexes of scopolamine; however, we are not prepared to accept this author's contention that the scopolamine test can be used as a means of detecting latent pyramidal lesions, as we have found that pyramidal symptoms can be induced by this drug given in an appropriate dose in normal subjects. A further study would be necessary to establish the normal "pyramidal tolerance," or "threshold" dose, below which the test would possess definite pathologic significance. We have interpreted the relative intolerance of epileptic patients to

23. Walshe, F. M. R.: Observations on the Nature of the Muscular Rigidity of Paralysis Agitans and on Its Relationship to Tremor, Brain **47**:159, 1924.

scopolamine (smaller dose required to induce pyramidal signs) as evidence of a merely relative deficiency or weakness of the pyramidal system in epileptics as compared to the normal.

Pseudobulbar Phenomena in Advanced Deterioration; Neurosomatic Deterioration in Epilepsy and in Presenile or Senile Arteriosclerotic Parkinsonism.—The blending of akinetohypertonic and bilateral pyramidal symptoms in more advanced cases creates a particular clinical picture. This picture consists in more or less pronounced pseudobulbar phenomena, such as spasmodic emotional incontinence, dysarthria, dysphonia and dysphagia. The pseudobulbar elements in the clinical picture of deteriorated epileptic patients are very common. In some cases they are merely suggested; in others they are more distinct, but in those cases which, on the background of an akinetohypertonic symptom-complex, develop bilateral pyramidal symptoms, the pseudobulbar elements are almost invariably present (cases 4, 5, 6, 7, 8 and 9).

The bilaterality of pyramidal symptoms seems to be an important and possibly an essential factor in the development of the pseudobulbar syndrome (Comte [24]). Yet Hughlings Jackson stated that double hemiplegia is not merely two hemiplegias, but that plus something else (quoted after Macdonald Critchley [25]). This "something else" is in large part pseudobulbar phenomena. The morbid physiology of the pseudobulbar syndrome is of great complexity.

The contributions of more recent years, especially of French and German authors (Brissaud, Comte, Pierre Marie, Oppenheim, Foerster, Lhermitte) tend to regard the pseudobulbar syndrome as a result of a combined involvement of extrapyramidal and pyramidal systems. It is almost self-evident that such an involvement must be due to a multiple or a diffuse lesion involving in particular the brain stem, such as lacunary disintegration, "état criblé," and similar degenerative or diffuse vascular pathologic processes affecting the brain. The mental changes, which are almost constant in pseudobulbar syndromes of whatever origin are attributed mainly to the cortical involvement by the same diffuse process.

In a recent paper on arteriosclerotic parkinsonism, Macdonald Critchley [25] once more brought forward the nonspecific character of this clinical syndrome as it is observed in certain arteriopaths. He described in this syndrome the parkinsonian or hypokinetic-hypertonic component, with masklike facies, muscular rigidity, characteristic posture and gait, and also a pyramidal spastic component, with exaggeration of reflexes of defense and of "affectivo-motor reactions" (Jarkowski [26]) and a

24. Comte, A.: Paralysie pseudo-bulbaire, in Nouveau traité de médecine, Paris, Masson et Cie, 1925, vol. 19, p. 451.

25. Critchley, Macdonald: Arteriosclerotic Parkinsonism, Brain **52**:23, 1929.

26. Jarkowski, J.: Kinésie paradoxale des parkinsoniens, Paris, Masson et Cie, 1925.

pseudobulbar component with emotional incontinence, spasmodic laughing and crying, dysarthria and dysphagia; in further advanced cases the "flexing factor" (Foerster) becomes more potent, contractures in flexion develop and eventually tendinous "retractures" set in, the patients becoming permanently bedridden.

According to the degree of development and combinations of these components in one clinical picture, the author isolates five types of the syndrome:

Type I: Characterized by rigidity, fixed facies, short stepping gait.

Type II: As in type I, with the addition of pseudobulbar manifestations (dysarthria, dysphagia and spontaneous laughter and crying) with two subtypes:

(*a*) Cases with signs of pyramidal disorder

(*b*) Cases without signs of pyramidal disorder.

Type III: As in type I, but with the addition of dementia, and incontinence of urine and feces.

Type IV: As in type I, with signs of pyramidal disease but without pseudobulbar manifestations (mixed pyramidopallidal syndrome).

Type V: As in type I, but with the superimposition of cerebellar symptoms (mixed pallidocerebellar syndrome) (Macdonald Critchley [25]).

Critchley specifies that there is a certain amount of overlap in this classification. It is evident that each type represents a more or less static aspect of one evolutive symptom-complex, so that each case can pass through the different phases; that is, a patient presenting a clinical picture, say of type I, in the further evolution of the condition can pass into type II or type III. When one compares the clinical aspects and evolution of arteriosclerotic parkinsonism with the clinical aspects and evolution of neurosomatic deterioration, certain analogies and differences at once attract attention. Critchley in his type V classifies cases with the superimposition on the pallidal symptom-complex of the cerebellar symptoms. Similarly, a cerebellar component could be considered also in the neurosomatic deterioration of epileptic patients. As this last variety of the deterioration possesses special interest in relation to myoclonus, we have reserved its discussion for the special topic of another paper.[27]

It is not difficult to see that the main elements of the symptomatology and evolution in pure arteriosclerotic parkinsonism ("arteriosclerotic deterioration") and in epileptic deterioration are essentially the same. These clinical analogies seem to suggest a similar topography of the pathologic process in both conditions. However, the origin and nature of the pathologic process is different. While in arteriosclerotic parkin-

27. Hodskins, M. B., and Yakovlev, P. I.: Clinical and Anatomico-Pathological Considerations on Myoclonus in Epileptics and on Related Symptom Complexes, to be published in the American Journal of Psychiatry.

sonism the onset of the clinical changes rarely takes place before the end of the fourth decade of life, in neurosomatic deterioration of epileptic patients the neurologic changes may develop in children (cases 4 and 6) and in young adults (cases 7 and 9), as well as in the aged (case 4). In young epileptic persons the evolution of the condition is on the average more rapid and more destructive (cases 6 and 7) than in persons in whom the symptoms develop in later life (cases 3, 4 and 8).

The nature and localization of the pathologic changes underlying the neurosomatic deterioration in epilepsy is of great interest. Information available from pathologic studies of the central nervous system of chronic and deteriorated epileptic patients so far is very meager. However, some data are at hand which, insufficient as they are for an adequate generalization, command at least a special orientation of pathologic thought. Courtois [18] in one case presenting the "syndrome comitio-parkinsonien," found at autopsy a diffuse cortical sclerosis and lesions of an inflammatory nature in a state of evolution affecting the region of the basal ganglia and medulla. He concluded that in many cases the "comitio-parkinsonien" syndrome is due to an old encephalitis, contracted possibly in the early life of the patients.

Urechia and Mihalescu [15] have found in an epileptic, aged 43, who had had epilepsy since early childhood and later developed a typical picture of a parkinsonian syndrome, degenerative lesions in the pallidal system and substantia nigra and moderate lesions in the other basal nuclei, without being able to determine from their pathologic observations the exact etiology of the lesions.

In a personal case, a boy, aged 13, developed a typical akinetohypertonic symptom-complex, with a parkinsonian facies and body attitude, generalized muscular rigidity, bilateral extensor response and pseudobulbar phenomena. The patient had been a full term baby. At 3 months he had had whooping cough; measles at 2 years; at 3½ years an acute illness of about one month's duration, with high fever; the condition was diagnosed as influenza with pneumonia (in 1918). He recovered, but a month later had a first epileptic attack. He died at 13 years of age following a series of convulsions. A histopathologic study of the brain, made in the laboratory of Dr. Stanley Cobb at Harvard Medical School, showed a diffuse gliosis with many degenerative and atrophic changes, especially in the third and fifth layers of the cortex, acute congestion, especially in the bulbar region, and marked evidence of an old inflammation with scar formation in the region of the basal ganglia and midbrain.

These few examples in which the clinical picture and pathologic observations were in agreement suggest that from the standpoint of localization the pathology of neurosomatic deterioration is in the first place a subcortical process. As to the origin and nature of this process, so far nothing precise is known. A study of a much larger pathologic material is necessary. One thing seems certain; the infections of the

central nervous system contracted in early childhood and the cryptic encephalitis of specific and nonspecific fevers, must play a more important and more general rôle in the pathology of epilepsy and of the subsequent neurosomatic deterioration than has been hitherto supposed. Of course, infections of the central nervous system do not exhaust the possible sources of the pathologic processes underlying epilepsy and deterioration. Primary or secondary degenerative and atrophic lesions (abiotrophies) are probably present in many cases. Cases of myoclonus epilepsy, especially of the familial variety (Unverricht-Lundborg type), constitute one example of this class. In the last place one must admit the influence of epileptic paroxysms which further aggravate and precipitate the evolution of a basic pathologic process in the brain, establishing in this way a circulus vitiosus.

1. Age limit	2 to 10	10 to 15	15 to 20	20 to 30	30 to 40	40 to 50	50 to 70
2. Number of cases	24	41	55	75	43	27	25
3. Average duration of epilepsy in years	4	9	10	16	23	26	22
4. Incidence of primary cerebral lesion	15 cases 62.5%	19 cases 46.3%	22 cases 40%	24 cases 32%	11 cases 25.6%	14 cases 51.8%	
5. Positive Babinski sign	54.2%	40.5%		17.5%	13%	32%	28%
6. Pyramidal symptoms including minor signs	91.7%	65.4%	45.4%	32.5%	28.3%	42.8%	36%
7. Cog-wheel sign	0%	12%		23%	20%	30%	
8. Exaggeration of the reaction of antagonists (triceps femoris)	28%	40%		52%	53%	55%	65%
9. Tremor	6%	10%		47%	51%	66%	
10. Clinical evidence of the extrapyramidal muscular hypertonia	33%	40%		48%	67%	52%	72%
11. Average frequency of grand mal seizures per month	9	7	5	4		3	2

RESULTS OF A NEUROLOGIC SURVEY OF A LARGE NUMBER OF AVERAGE INSTITUTIONAL CASES OF EPILEPSY

The nine observations cited at the beginning of this paper were selected from a large number of cases in order to facilitate the presentation of a rather complex subject. Our experience actually was based on the neurologic survey of a much larger material. The study of the neurologic changes observed in epileptic patients was started three years ago, and at the present time the number of patients observed is over 500. The first series of recorded observations was submitted to a statistical study. This series consisted of 290 cases which represents the average material of a large institution. These cases were selected because the

patients were physically fit to come to the examination room without assistance, and were in relatively good mental condition so that they gave at least a minimum collaboration during the examination. The statistical analysis of the recorded observations was made in an attempt to obtain, at least in a crude form, a more general insight into the nature of the material studied and into the relationship of certain more common and more prominent clinical symptoms to such factors as the age of the patients, the duration of the epilepsy, the frequency of convulsions, and finally, the incidence of a primary cerebral lesion evident either from both clinical examination and from previous history, or only from the latter. We have arranged 290 case records according to the age of the patient in several successive groups and have noted the average duration of epilepsy for each group as given in lines 1, 2 and 3 of the accompanying table.

In a series of 265 case records of patients from 2 to 50 years of age, we found in about 40 per cent that there was unquestionable evidence that at some time previous to the onset of epilepsy there had been a diseased condition directly involving the central nervous system (106 cases). These cases can be classified, therefore, as "symptomatic." The various diseased conditions responsible for these primary cerebral lesions can be grouped under the following headings:

(1) Acute encephalitis or meningo-encephalitis of childhood of various etiology, 26 cases (9.8 per cent).

(2) Epidemic encephalitis, 12 cases (4.5 per cent).

(3) Meningitis and meningeal complications of extracerebral diseases (otitis purulenta, etc.), 9 cases (3.2 per cent).

(4) Cerebral complications of pulmonary tuberculosis (tuberculoma or tuberculous pachymeningitis), 1 case.

(5) Acquired syphilis with evidence of syphilitic meningitis or meningo-encephalitis, 2 cases (0.8 per cent).
Total of acute or chronic infections of the central nervous system, 51 cases (19.2 per cent).

(6a) Hereditary syphilis with serologic evidences, 11 cases (4.2 per cent).

(6b) Hereditary syphilis without serologic evidence, but with clinical evidence, 10 cases (3.8 per cent).
Total, 21 cases (8 per cent).

(7) Birth complications (only cases with epilepsy following immediately or within a few days after birth were considered), 15 cases (6 per cent).

(8) Craniocerebral traumatism in subsequent years of life and previous to the onset of epilepsy, 12 cases (4.5 per cent).

(9) Cerebral tumors, 3 cases (1 per cent).

(10) Chronic alcoholism, 3 cases (1 per cent).

In 159 cases the previous history did not contain sufficient evidence of the occurrence of such primary cerebral lesions. Thus, these 159 cases were what is ordinarily called "genuine epilepsy." In the table, at

line 4, we give the incidence of primary cerebral lesions in the respective age group. Following the incidence of the primary cerebral lesion we find that the lesion is of very common occurrence in younger groups of patients, rapidly becomes less frequent in the older groups and becomes more frequent again in the group of the fifth decade.

We have shown in the previous paragraph that in the clinical evolution of deterioration the pyramidal symptoms become associated with the akinetohypertonic symptom-complex, marking the further advanced phase of deterioration. Unless present as part of the residual syndrome of a primary cerebral lesion, the pyramidal symptoms do not stand in the foreground of progressive neurosomatic deterioration as they are common only in the more advanced cases. We have determined the incidence in the successive age groups of an extensor response (Babinski sign) as a most characteristic and unmistakable symptom of a pyramidal lesion. The incidence of a Babinski sign is given in the table at line 5 in percentage figures of the total number of cases of the respective groups. In line 6 is given the incidence of pyramidal symptoms in general, that is, taking account also of minor pyramidal signs (Oppenheim sign, foot clonus, combined flexion sign, etc.). Taking into account these figures, one can observe that the incidence of pyramidal symptoms runs fairly parallel to the incidence of primary cerebral lesions, illustrating the dependence of the pyramidal symptoms on the presence of such a lesion.

We have already pointed out, in discussing the series of typical cases, that in the evolution and symptomatology of neurosomatic deterioration the akinetohypertonic symptom-complex is the basic component. We have estimated the incidence of certain more common and more prominent intrinsic clinical signs of increased muscular tonus.

The cog-wheel sign of Camillo Nigro is one of the unquestionable evidences of muscular rigidity. At line 7 in the table are given the figures of the incidence of the cog-wheel sign in respective groups of cases. One can observe that these figures become progressively higher in the groups of older patients.

The exaggeration of the reaction of antagonists is another clinical criterion of muscular hypertonia. The incidence of the exaggeration of the antagonistic contraction of the triceps femoris is shown in the table on line 8. The incidence of this clinical symptom shows a steadily progressive increase from the younger to the older patients.

Tremor of the tongue, hands and fingers is commonly accepted as a sign of disorder of tonic innervation. The respective figures of the incidence of tremor in successive age groups are given at line 9, which show the same behavior as the other hypertonic symptoms.

Finally, at line 10 of the table, is given the percentage of cases presenting symptoms indicative of muscular rigidity, that is presenting more or less distinct evidence of the akinetohypertonic symptom-complex.

From the figures in lines 7, 8, 9 and 10, one can see that the incidence of symptoms of akinetohypertonic type (muscular rigidity) shows that there is a distinct parallelism between the incidence of the hypertonic symptoms on one hand and the age of the patient (line 1) and duration of epilepsy (line 3) on the other. In the older patients, with the longer average duration of epilepsy, the incidence of hypertonic symptoms becomes higher.

The numerical formulation of the results of the neurologic survey of a large number of average institutional cases shows clearly that the symptoms of the akinetohypertonic type are a more specific expression of progressive neurosomatic deterioration than symptoms of the pyramidal series. These observations tend to localize the pathologic process underlying the progressive neurosomatic deterioration of epileptic patients rather in the subcortical level than in the cortical level as has hitherto been the general tendency.

We have already mentioned the observations of several authors that in some epileptic patients the development of a pronounced degree of muscular rigidity of parkinsonian type often coincides with a noticeable decrease in the frequency of convulsive paroxysms (Urechia and Elekes,[15] Courtois,[18] Marchand and Courtois,[28] Yakovlev [17]). In line 11 of the table are given figures of the average monthly frequency of grand mal seizures per case in the successive groups. The number of convulsions in each case was taken from the month when the patient was examined. The distinct decrease of the average frequency of convulsive seizures with the greater incidence of muscular rigidity is clearly demonstrated by these figures.

In the lack of a better explanation for this peculiar diminishing of convulsions, often coinciding with the progress of rigidity, the following hypothesis seems plausible: Assuming that the progressive rigidity—the epileptic parkinsonism—is a clinical expression of the functional deficiency of the subcortical centers, one is tempted to infer that with the progressive deficiency—wearing out—of these subcortical centers the convulsive capacity diminishes.

In connection with this hypothesis it is not without interest to mention that such drugs as phenobarbital, the anti-epileptic action of which is generally known, according to recent researches of Keeser [29] show an elective affinity for the brain stem centers. In animals poisoned with a barbituric acid compound, this substance was never found in the cortex, cerebellum or medulla; on the contrary, rich amounts of this substance were found in the corpus striatum and thalamus. It appears,

28. Marchand and Courtois: De l'épilepsie dite "sous-corticale," "striée," ou "extrapyramidale," Rev. neurol. **2**:31, 1929.

29. Keeser, quoted by Molitor, H., and Pick, E.: Pharmakologie der Schlafmittel, in Sarason: "Der Schlaf," München, J. F. Lehmanns, 1929.

therefore, that phenobarbital is electively soluble in the lipoids of the brain stem centers and is not soluble in the cortex, cerebellum or medulla. On these grounds, phenobarbital and other compounds of the barbituric acid group are classified as brain stem hypnotics. It is possible that the anti-epileptic effect of phenobarbital depends on the same elective toxic action on the subcortical centers.

Purely clinical concepts do not submit themselves readily to a statistical formulation we have used, however, a numerical method to express the incidence of certain clinical phenomena as the changes in the figures obtained from one group of cases to another group, and from one series of clinical phenomena to another series, showed a distinct relationship to certain constant factors (age, duration of epilepsy, primary cerebral lesion) which we believe is of considerable interest, at least inasmuch as this relationship gives definite orientation for further research.

SUMMARY

Neurosomatic deterioration in chronic epilepsy is a clinical concept derived from the study of a large number of epileptics in a special institution. Being of a most heterogenous nature, these cases possess two common features—epileptic paroxysms and progressive deterioration. The present study was concerned with the progressive neurologic changes developing in the course of deterioration.

The modification of the muscular tonus (rigidity of extrapyramidal type) and of posture are the outstanding elements of an akinetohypertonic symptom-complex which is the basic clinical expression of progressive neurosomatic deterioration. On the background of the akinetohypertonic symptom-complex (epileptic parkinsonism, syndrome comitio-parkinsonien) are observed: (1) progressively developing and eventually bilateral symptoms of the pyramidal series with spasticity predominating in the lower extremities; (2) progressively developing symptoms of pseudobulbar type with contractures in the lower extremities and a tendency to a flexion attitude (clasp-knife posture of the body); (3) ultimate flexion paraplegia of cerebral type with tendinous retractions and advanced dementia.

These neurologic changes, developing in the course of neurosomatic deterioration, are different in nature and independent in their clinical evolution from the residual syndromes (sequelae) of primary cerebral lesions (infantile hemiplegia, etc.) so often found in epileptic patients.

The symptoms of akinetohypertonic type and the symptoms of pyramidal type exhibit a sort of reciprocal antagonism, the rigidity counteracting the amplitude of reactive movements (reflexes of defense, emotional reaction to painful stimuli) and intensifying the tonic postural reflexes, while the pyramidal spasticity exaggerates the reflexes of de-

fense and the spasmodic emotional reactions (emotional hyperalgesia) but at the same time diminishes the tonic postural reflexes.

After the injection of scopolamine hydrobromide, muscular rigidity disappears, hypotonia develops instead, and tonic postural reflexes are abolished, while pyramidal symptoms become elicitable. The same effect is observed in normal persons as in epileptic patients but a relatively higher dose of the drug is required in the former. The relative intolerance of epileptic patients to scopolamine can be regarded as an evidence of relative deficiency or weakness of the pyramidal system in epileptic as compared with normal persons.

The nature and localization of the pathologic process underlying the neurosomatic deterioration of chronic epileptic patients is not sufficiently known. However, clinical analogies of the symptomatology, and especially of the evolution of the deterioration of epileptic patients with the symptomatology and evolution of arteriosclerotic parkinsonism (arteriosclerotic deterioration), and the few available histopathologic studies bring us to regard the pathologic process underlying neurosomatic deterioration as primarily a subcortical process, gradually becoming more diffuse and more destructive.

The results of a neurologic survey of a large number of average institutional cases of epilepsy tends to show that the symptoms of akinetohypertonic type are a more specific expression of deterioration than the symptoms of pyramidal type.

EPILEPTIFORM CONVULSIONS

THE INCIDENCE OF ATTACKS IN CASES OF INTRACRANIAL TUMOR *

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In some cases of intracranial tumor epileptiform convulsions occur, and in other cases this symptom is entirely absent. Tumors involving the brain do not produce a clearcut sequence of cause and effect as seen in other pathologic processes. The symptoms and signs produced by tumor are extremely variable, inconstant to a marked degree and altogether inconsistent. Nevertheless, when approached with due caution and reserve, the problem is fascinating in spite of its bewildering inconsistencies.

From the records of patients who had come to the Mayo Clinic from Jan. 1, 1919, to Nov. 1, 1929, 313 cases of intracranial tumor were found in which complete clinical studies had been made and necropsy data had been assembled. It may be assumed that the group is fairly representative of the incidence of intracranial tumor in the general population. The criticism might be made that only cases in which death had occurred were taken; necessarily, therefore, some more malignant types of process were present. Death, however, is common in cases of tumor of the brain, and even if in the group were included those cases in which the conditions have been relieved by surgical procedures, or patients who later died elsewhere or who are still under observation, the general frequency and incidence of the various types of tumor would be changed but little. It is a distinct advantage to deal only with cases in which the diagnosis is definitely established, the anatomic situation of the tumor known and the histologic character of the growth determined.

Search was made in the records of these 313 patients for evidence of occurrence of major epileptiform seizures at some time before death. Such manifestations as syncopal attacks, periods of stupor, petit mal, tonic spasms and jacksonian convulsions without loss of consciousness were excluded. The question as to what is included under the term of major epileptic seizure might be raised, but since the definition is so loose and individual variation in convulsions so great,

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* From the Section on Neurology, the Mayo Clinic.

*Read before the Association for Research in Nervous and Mental Diseases, New York, Dec. 28, 1929.

personal judgment as to what constitutes a general convulsion must be accepted. There was little difficulty in finding good records, for such a phenomenon as a general convulsion is sufficiently startling to impress itself indelibly on the minds of observers, both lay and medical. After a process of search, selection and exclusion, sixty-seven cases were assembled which fulfilled all requirements (chart 1). This represents a percentage of 21.6 of the total, and is midway between Sargent's [1] 30 per cent for 270 cases and Dowman and Smith's [2] 19 per cent for 100 cases. Dana's [3] estimation of convulsions in a fourth of all cases of cerebral tumor is somewhat higher than in my series, and MacRobert and Feinier's [4] figure of 4 in 165 (2.4 per cent) is somewhat low for the general run of cases. However, in my series it was not the percentage of cases of intracranial tumor in which convulsions occurred that is striking, but the fact that there were so many cases in which nothing suggested such a symptom even though the disease

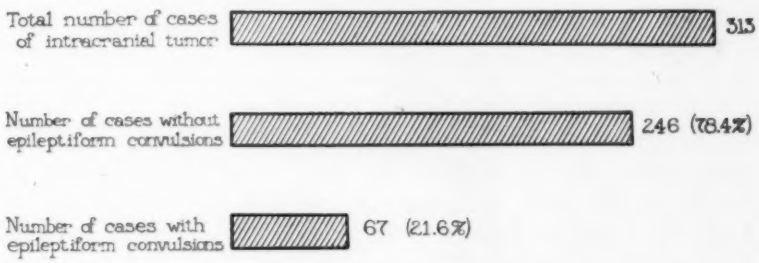


Chart 1.—The number and proportion of cases of intracranial tumor in which convulsion occurred.

processes seemed to be identical. The next step was to classify all the cases of tumor with regard to their anatomic situation, and on this background to estimate the relative frequency of convulsions in cases of tumor in different situations. In each instance the site of the tumor was indicated by the region involved by the greatest visible mass of tumorous tissue. It is readily understood that sharp boundary lines often do not occur in tumors of the brain, especially the infiltrating subcortical type. Where the tumor ends and the normal brain begins, and how far the surrounding zone of softening, when it exists, may extend, are difficult to determine at any time. Actually the extent of the

1. Sargent, Percy: Some Observations on Epilepsy, Brain **44**:312, 1921.

2. Dowman, C. E., and Smith, W. A.: Intracranial Tumors: Review of a Hundred Verified Cases, Arch. Neurol. & Psychiat. **20**:1312 (Dec.) 1928.

3. Dana, C. L.: Textbook of Nervous Diseases, New York, William Wood & Company, 1925.

4. MacRobert, R. G., and Feinier, Laurent: Cerebellar Fits, Arch. Neurol. & Psychiat. **5**:296 (March) 1921.

growth may be impossible to estimate even with the microscope. Accordingly, for such a study, gross estimations of the site, extent and size of the tumor must be accepted.

Chart 2 shows the general incidence of tumors for various situations in the cranial cavity. In my series, tumors involving the frontal lobes represented 16 per cent of the total number of cases and a greater percentage than any other group of tumors situated elsewhere. Not

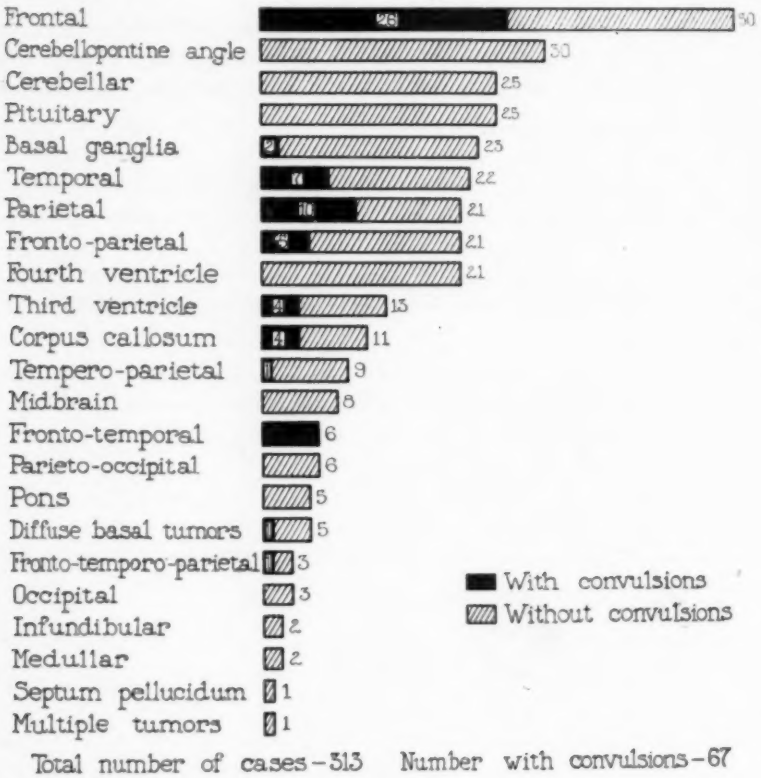


Chart 2.—The incidence of tumors in various situations within the cranial cavity and the incidence of accompanying convulsions.

only was the general incidence of tumors involving the frontal lobes high, but of the fifty cases of tumors in this region, convulsions occurred in twenty-six (52 per cent). Furthermore, this represents a large proportion (38.8 per cent) of all the cases of intracranial tumor in this series in which convulsions were a symptom. Müller [5] estimated that convulsions occur in a third of all cases of tumor of the frontal

5. Müller, Eduard: Zur Symptomatologie und Diagnostik der Geschwülste des Stirnhirns, Deutsche Ztschr. f. Nervenh. **22**:375, 1902.

lobe, but Sargent's figures more closely agree with mine. He found that in forty-one of eighty-two cases of intracranial tumor and convulsions, the lesion was situated in front of the central sulcus. In Dowman and Smith's series, in fourteen of nineteen cases the tumor was of the frontal lobe. The significance of lesions of the temporal lobe in producing convulsions has been emphasized in the past. Kennedy [6] found that convulsions had occurred in seven of nine cases of tumor involving the temporal lobe. Cushing's [7] figures, however, more closely approximate those in my series. He found that in only twenty of fifty-nine cases of tumor of the temporal lobe had convulsions occurred; this represents about 34 per cent. In my series, convulsions occurred in seven of twenty-two cases of tumor of the temporal lobe (approximately 31.8 per cent). Convulsions were more common when the tumors were in other situations, such as the frontal lobe, already mentioned, but also in the parietal lobe and the corpus callosum. In cases in which the tumor involved other portions of the brain along with the temporal lobe, there was an even greater incidence of convulsions than in cases in which the tumor involved the temporal lobe alone. The number of available cases was small, and it is not justifiable, therefore, to lay much stress on this. Nevertheless, convulsions were recorded in six cases of tumor involving both the frontal and the temporal lobes, and in one of three cases of tumor involving the frontal, temporal and parietal lobes.

Altogether, in terms of the total of sixty-seven cases with associated convulsions, those in which the tumor involved the frontal, parietal and temporal lobes, singly or in combinations, tended to outnumber all others, in the proportion of 5:1 (chart 3). The other cases, nevertheless, are of interest and include cases of tumor in the median line. Although convulsions are relatively more common in association with tumors involving the cerebral hemispheres those in the third ventricle, basal ganglia and corpus callosum have a certain definite representation.

The outstanding feature of the study was the complete absence of major epileptic seizures in cases of tumor below the tentorium (chart 4). This has been commented on elsewhere.[8] Collier [9] suggested a

6. Kennedy, Foster: The Symptomatology of Temporosphenoidal Tumors, Arch. Int. Med. **8**:317 (Sept.) 1911.

7. Cushing, Harvey: Distortions of the Visual Fields in Cases of Brain Tumor: The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341, 1922.

8. MacRobert and Feinier (footnote 4). Stewart, T. G., and Holmes, Gordon: Symptomatology of Cerebellar Tumors: A Study of Forty Cases, Brain **27**: 522, 1904.

9. Collier, James: The False Localizing Signs of Intracranial Tumor, Brain **27**:490, 1904.

few exceptions, but these were in cases in which the lesion was far advanced. Increase in intracranial pressure is fairly well excluded as a factor in the production of convulsions in cases of intracranial tumor, for infratentorial tumors are more commonly associated with increased intracranial pressure than are supratentorial tumors. The converse also

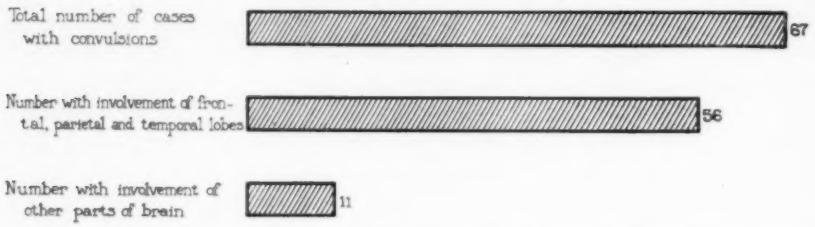


Chart 3.—Incidence of tumors in frontal, parietal and temporal lobes, taken together, compared with incidence of tumors in other regions of the brain.

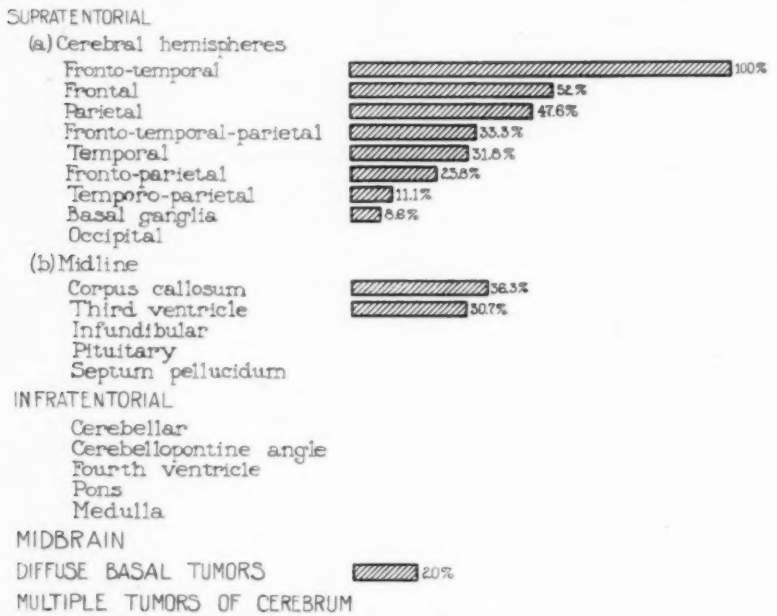


Chart 4.—The proportion of cases in which convulsions accompanied tumors in various regions of the brain.

holds, for in the sixty-seven cases in which convulsions occurred, thirty-three did not disclose evidence of increased intracranial pressure as far as ophthalmoscopic examination of the eyegrounds was concerned.

From the study of the sixty-seven cases of intracranial tumor in which convulsions were associated, some general deductions may be

made as to the part the situation of the tumor plays. Furthermore, it is possible, in a case of intracranial tumor in which convulsions appear as a symptom, to assume certain regions of the brain to be the possible site of the lesion. Thus the occipital lobe, the midbrain and all structures below the tentorium play only a small part. Farther forward in the brain, however, is the site of the tumors accompanied by general convulsive seizures. Sargent stated that the nearer a tumor or its surrounding area of softening approaches the central sulcus, the more likely are convulsions to occur, but necessarily in this study I included also the lateral fissure. Tumors involving the frontal, parietal and temporal lobes, in descending order of frequency, by far outnumber, in the incidence of associated convulsive seizures, the tumors situated elsewhere in the cranial cavity.

Of the sixty-seven cases of tumor associated with convulsions, twenty-five tumors were on the right side, thirty-three were on the left and nine were in the median line. There is, therefore, no predominance of one side over the other. It was hoped that some influence might be discovered to be exerted by the histologic structure of the tumor. Accordingly, the tumors were classified as extrinsic and intrinsic as far as their origin was concerned. It is convenient to regard as extrinsic those tumors arising outside the brain: from its bony or membranous covering, or from the cranial nerves. These naturally include, for the most part, meningiomas and neurofibromas. The intrinsic tumors are chiefly the infiltrating gliomas of various types, ependymomas and tumors arising from the blood vessels and connective tissue in the substance of the brain. From the whole group of supratentorial tumors, a subgroup, composed of those in which the patients have convulsions, was separated. The ratio of patients who had extrinsic tumors to those who had intrinsic tumors was about the same in the whole group and in the subgroup made up of those who had convulsions (chart 5). Possibly the percentage incidence of extrinsic tumors is slightly higher among cases in which seizures occur.

Another phase of the problem is the study of the course of the disease in respect to the appearance of the convulsions. Whenever an adult patient appears for examination complaining of recently acquired convulsions, there is ever a lurking dread in the mind of the examiner that this symptom represents the initial phase of an intracranial tumor. At times it is not possible to exclude tumor, and the miserable process of waiting for further signs of growth is frequently enforced on both patient and physician, with anxiety and misunderstanding on one side and a sense of inferiority and chagrin on the other. Encephalography or ventriculography often helps to overcome this sufficiently to permit an earlier diagnosis. Nevertheless, it is worth asking the question as

to how frequently an intracranial tumor announces its presence for the first time by a convulsive seizure, and how long the average case must progress before definite signs of tumor appear. It is well known that a patient may have convulsions for many years before unmistakable evidence of cerebral tumor appears, but it is of interest to inquire how often this occurs in comparison with cases in which symptoms of cerebral tumor appear either simultaneously with the first convulsion or soon afterward, and, also how often convulsions are a late or even terminal phenomenon in cerebral tumor.

Among the sixty-seven patients with cerebral tumor and major epileptic seizures, there were thirty-eight in which the convulsion was the first sign of disease. In fifteen of these, simultaneously with this initial convulsion or shortly afterward, the whole clinical syndrome of intracranial tumor rapidly unfolded itself, and events happened in

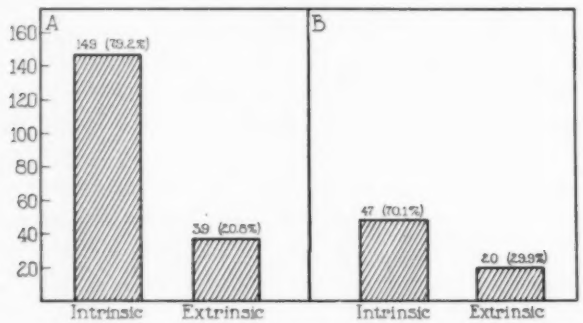


Chart 5.—Incidence and proportion of intrinsic and of extrinsic tumors: *A*, in the whole group of supratentorial tumors; *B*, in the subgroup of supratentorial tumors composed of those which were accompanied by convulsions.

definite sequence, leading to a fatal termination. There were, however, twenty-three other cases in which a latent period occurred with no more symptoms than intermittent convulsive seizures to indicate grave cerebral disease. In ten of these cases, however, more signs of cerebral tumor developed within a year. Thus, in thirteen cases seizures occurred for more than a year without other signs of cerebral tumor. The longest duration in these cases before other symptoms of tumor appeared was twenty-three years; in two other cases it was seventeen and fifteen years, respectively. In the first of these three cases a meningioma with overlying osteoma was present in the left frontal region; in the second case, a glioma in the right frontal region, and in the third case, a glioma in the rostral portion of the corpus callosum. Apart from these three cases in which the history was excessively long, there were ten others in which the average duration of the history without signs of tumor other than convulsions was five

and six-tenths years. In four of these cases the duration had been nine years, and no doubt all thirteen cases had masqueraded as cases of epilepsy during the years that had passed before signs indicating the real nature of the disease appeared. Altogether, these thirteen cases represent 4.1 per cent of the total series of cases of intracranial tumors. Accordingly, in this 4.1 per cent, it is possible that convulsions antedated for years the appearance of other signs leading to a correct diagnosis. From another point of view can be considered the incidence of cerebral tumor found at necropsy in institutionalized epileptic patients. At Craig Colony it was 2 per cent, and in Australia it was 3.5 per cent.[10] Lennox and Cobb, in a study of a large series of noninstitutionalized adult epileptic patients, found the incidence of tumor to be 3.5 per cent.[11]

In only twenty-nine of the sixty-seven cases did aura occur as a prodrome to the attack. As might be expected, when present it was either motor or sensory, or both; it was referred to the extremities in eighteen of these cases. The motor aura was frequently jacksonian but in two cases there was elevation of the whole arm and leg on one side just before the patient fell in a convulsion. In five cases of left-sided tumor the aura was aphasic as well as motor or sensory, and in three cases of tumor of the temporal lobe there was a gustatory or olfactory aura. The various combinations of aura—motor, sensory, aphasic or olfactory—were diagnostic in the extreme when present and served a good purpose in indicating a gross cerebral lesion.

From the standpoint of diagnosis of cerebral tumor, the convulsions at some period of the disease differed not at all from those seen in epilepsy, but the tendency toward a change in type is suggestive. A patient may start out with jacksonian convulsions, and later general attacks may develop, or vice versa. The character of the aura also helps in establishing a diagnosis. A march of events from attacks of paresthesia and later motor convulsions, finally leading to generalized convulsions sooner or later, was also seen a number of times. Although 4.1 per cent of cases of intracranial tumor began with a convulsion without any other signs for several years, there was necessarily a much larger percentage of cases in which unmistakable evidence of intracranial tumor was already present or in which more and more signs of cerebral injury developed immediately or soon after the initial convulsion. Occasionally the only convulsion that occurred was at the

10. Lennox, W. G., and Cobb, Stanley: Epilepsy, Baltimore, Williams & Wilkins Company, 1928.

11. Lennox, W. G., and Cobb, Stanley: The Non-Institutional Epileptic: A Preliminary Report of the Association's Co-operative Study, Presented before

onset of the disease and was never repeated. In two cases death occurred during a series of convulsions which were the only convulsions that were experienced. The common feature, however, in cases of intracranial tumor, is that the patient is generally worse after such a convulsion, recovers a little, then goes downhill again after the next convulsion or series of convulsions, and finally the convulsion is only a small part of the general symptomatic picture.

Generally speaking, therefore, there are in the majority of cases of cerebral tumor and convulsions some features that lead to the current diagnosis and help to distinguish the case readily from one of epilepsy.

As to the mechanism by which convulsions occur in cases of intracranial tumor, nothing is definitely known. Too few such patients are afflicted by convulsions even to constitute an argument for direct cause and effect. From the truth of the particular it is manifestly illogical to infer the truth of the universal, and, as Sargent stated, there is no gross lesion of the brain, traumatic or otherwise, which necessarily causes convulsions. Lennox and Cobb also drew attention to the relatively small number affected, and suggested that there is some factor other than the tumor which is responsible for the convulsions. The theory advanced by MacRobert and Feinier, that tumors in the temporal lobe produce convulsions by intermittently squeezing the middle cerebral artery, is fascinating, but tumors in other situations are even more likely to be associated with convulsions. In my series, large areas of infarction surrounded some of the tumors in cases in which convulsions had not occurred. In one case previously reported by me, a small tumor at the tip of the temporal lobe had presumably compressed the middle cerebral artery and thereby had produced a massive area of infarction; although a large portion of the cerebrum had become anemic, infarcted and softened, convulsions had not occurred. On the other hand, it is a frequent clinical observation that sudden occlusion of the middle cerebral artery by an embolus may bring on a series of general epileptiform convulsions ushering in the hemiplegia produced by the infarction. Sargent also favored the idea that some disturbance of the vascular supply in the neighborhood of the tumor might be responsible for the convulsions accompanying its course. He admitted that cerebral tumors do not necessarily produce convulsions, but stated that rapid and sudden alterations of vascularity can take place in and around them and be held responsible for a convulsion. Whatever theory is used, it must take into consideration that for every tumor associated with convulsions, one or more others can be produced which are identical in their histologic structure and their anatomic situation without the slightest evidence of convulsive attacks appearing before death. As has been mentioned, this inconsistence is common in cases

of tumor of the brain. Normality of function may be surprisingly well preserved in the face of massive growths, both extrinsic and intrinsic to the brain, with extreme anatomic derangement. Before the problem of convulsions associated with intracranial tumors and the exact relation between the two can be settled, further work must be done on the influence of tumors on the substance of the brain and the mechanics of the production of symptoms in such diseases.

SUMMARY

In 313 cases of intracranial tumor with complete data from clinical sources and from necropsy, 67 (21.6 per cent) were found in which major epileptic seizures had occurred. All of the intracranial tumors associated with convulsions were situated above the tentorium. In most of the cases (56) in which convulsions occurred, the tumor was situated in the frontal, parietal or temporal lobes of the brain, in descending order of frequency, or in various combinations of these areas.

Convulsions occurred as an initial symptom of the disease in thirty-eight cases. In thirteen cases no other complaint had been present for one or more years preceding the development of other signs and symptoms. The actual proportional number of cases in which convulsions occurred as compared with the total number was too small from which to draw any conclusions as to the part intracranial tumors play in the production of convulsions.

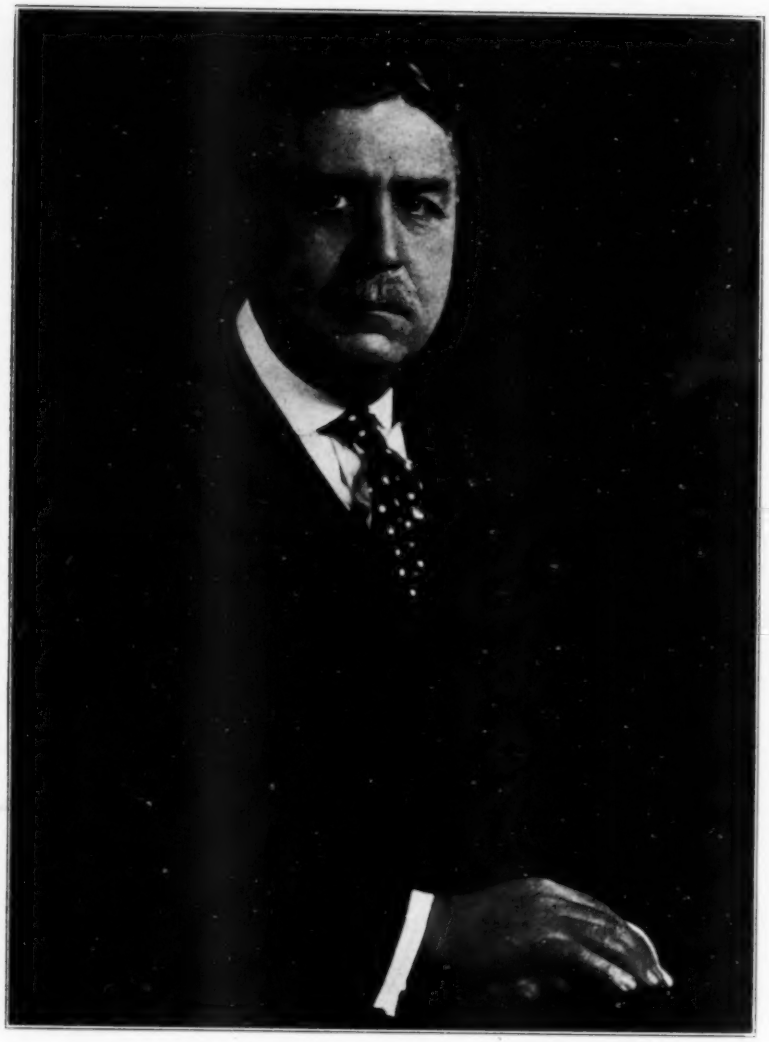
News and Comment

A MENTAL HYGIENE INSTITUTE

A Mental Hygiene Institute, in the form of a Summer School, is planned for the three weeks from June 30 to July 19, 1930. The course will be held at the Connecticut College, New London, and arrangements are being made to accommodate those who wish to attend. It is being planned for visiting nurses, teachers, social workers, probation officers, physicians and others of sufficient educational background. There will be no charge for tuition, and expenses connected with the Institute will be at a minimum. Those interested should communicate with the Division of Mental Hygiene, State Department of Health, Hartford, Conn.

CORRECTION

In the article by Dr. Harry A. Paskind on "Manic-Depressive Psychosis in Private Practice," in the April issue (**23**:789, 1930), the legend for chart 1 should refer to four hundred and forty-four, instead of to forty-four, attacks. The interval referred to by the author in the first sentence in his closing discussion should be forty-four, instead of four, years.



CHARLES SOWER POTTS, M.D.
1864-1930

Obituaries

CHARLES SOWER POTTS, M.D.

1864-1930

Ever since he was a member of the '85 varsity crew at the University of Pennsylvania, during seasonable weather Dr. Potts could be seen each afternoon in a racing shell on the beautiful Schuylkill River in Fairmount Park, Philadelphia. He rarely took a vacation, for one of his chief delights was to turn in each year one of the best logs for miles on the river. At the age of 66 there was not a gray hair in his head, and he seemed robust and well. It was therefore with a great deal of misgiving that his friends noticed that he lacked his usual energy during the summer of 1929. In October, he was confined to a hospital, and died from a cerebral condition on Feb. 16, 1930.

Dr. Potts was a direct descendant of David Potts who settled in Philadelphia before the arrival of William Penn. He received his early education at the Central High School and the college department of the University of Pennsylvania, and graduated from the medical department in 1885. Following an internship in the Philadelphia General Hospital, he spent the first few years of his professional life in the coal regions of Pennsylvania. He then became associated with Dr. Horatio C. Wood in the department of neurology at the University of Pennsylvania, where he finally became associate in neurology. In 1907, he was made professor of nervous diseases in the Medico-Chirurgical College, and on the merging of this institution with the Graduate Medical School of the University of Pennsylvania, he became professor of nervous diseases in the latter institution, holding this position at the time of his death.

Dr. Potts held many important hospital positions. He was always greatly interested in the neurologic wards of the Philadelphia General Hospital, where he was attending neurologist. He was also on the staffs of the Lankenau Hospital and the Graduate Hospital, and was consulting neurologist to the Atlantic County Hospital for Mental Diseases and to the Eastern Penitentiary. He was a member of many organizations, among them the College of Physicians, Philadelphia, the Philadelphia Neurological Association, the American Neurological Association, the American Psychiatric Association.

Dr. Potts was a large contributor to the neurologic literature and was the author of several popular textbooks, one entitled "Nervous and Mental Diseases" and another, "Medical Electricity."

Outside of his medical activities Dr. Potts had many other interests. Historical research, particularly the colonial history of Pennsylvania and the New England States, aroused his attention. He was much interested in general literature and at one time possessed a most extensive general library. He was greatly interested in music, being a regular attendant of the Philadelphia Orchestra Association.

The patients in the nervous wards of Old Blockley saw another side of him. It is to be recalled that these wards are made up of the poor of Philadelphia. Dr. Potts had an extensive collection of phonograph records. For many years it was his habit to go there every few days and to give these patients a concert, and it is not at all surprising that he bequeathed his phonograph and records to the nervous wards.

His friends, however, in remembering him, will think of his human side. He had a rather abrupt and brusque manner which hid the gentlest of souls. At no time was he afraid of saying exactly what he thought. His word could always be depended on. If he ever had a grievance, he came out with it. It was pleasant to deal with a man of his sort.

Few men had more friends, and they will always remember him as one of the squarest men that ever lived.

WILLIAM HOUSE, M.D.

1873-1930

WILLIAM HOUSE, M.D.
1873-1930

On March 6, 1930, following an illness of months, Dr. William House died at his home in Portland, Ore. He was born in Ellenville, Ulster County, New York, on Nov. 8, 1873, and received his medical degree from the University of Buffalo in 1895. Following an internship in a general hospital, he became resident physician in the Erie County (N. Y.) Hospital (1895-1896) and later assistant physician in the Manhattan State Hospital for the Insane, Ward's Island, New York (1896-1897). In 1898, he was assistant in anatomy in the medical department of the University of Buffalo. In 1903, he settled in Portland, and there remained to make his home, specializing in neuropsychiatry.

Dr. House made an eminent success of his life and his specialty in its broadest sense. Although the demands of his private practice were great, he found time for scientific research and contributed numerous articles in his special field. His early scientific writings dealt chiefly with clinical problems in neurology, but in later years his publications were along psychiatric lines. From this later bibliography may be mentioned: Occultism and Insanity, The Patient's Mind, and Socio-Economic Problems in Neuro-Psychiatry, which, in addition to mature and discerning discussion of these problems, showed a high degree of literary merit.

He was an active teacher, occupying the position of assistant professor and associate professor of nervous and mental diseases (1905-1920) and as professor of medical jurisprudence (1908-1920) in the Oregon University Medical School.

He was the recipient of many honors testifying to the esteem and professional regard in which he was held by his medical colleagues. Among these may be mentioned: secretary of the Oregon State Medical Society, 1908-1911; president of the Portland City and County Medical Society, 1912-1913; president of the Portland Academy of Medicine, 1923. In 1926-1927, he was chairman of the Section of Nervous and Mental Disease of the American Medical Association. He was a member of the American Psychiatric Association and of the American Neurological Association; he became a member of the latter organization in 1923. He was on the visiting staff of the Good Samaritan Hospital, St. Vincent's Hospital, and visiting neurologist for the Multnomah Hospital in Portland.

Dr. House was gifted with a felicity of expression and a happy humor which made him much sought after as a speaker in social and medical gatherings. He was devoted to his family and ever solicitous of their happiness and welfare.

A loyal friend, generous of himself to those who needed him, he died in the bloom of his career, and will be sadly missed in his community as friend, counselor and physician.

Abstracts from Current Literature

A Clinical and Pathogenetic Study of Spontaneous Movements Associated with Disturbances of Sensibility. Erwin Stengel, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:649 (Aug.) 1928.

Spontaneous movements are of two types: (1) The episodic, cramplike, cursory movements, described chiefly in tabes, and associated with pains or other sensory disturbances. These movements are looked on as typical motor responses to abnormal sensory stimuli. (2) The spontaneous movements of a more or less constant nature, the so-called pseudo-athetotic movements described chiefly in tabes. Oppenheim described athetosis-like movements in disturbances of deep sensation and in cerebellar cases, differing from true athetosis in their sameness and stereotyped form. Lewandowsky pointed out that these movements are noticeable when the ataxia involves the arms and that they are difficult to distinguish from static ataxia, and Oppenheim gave them the noncommittal name of spontaneous movements. Herman later showed that these movements may occur in all patients with disturbance of deep sensation, whether of a peripheral or a spinal origin, and that they are the result of deep sensation. He called them pseudo-athetotic spontaneous movements. Erben looked on them as an important component of tabetic ataxia, and assumed that they represented a loss of orientation of the position of the extremities and joints. Guillain, Alajouanine and Girot have recently described three groups of spontaneous movements in tabes: (1) non-rhythmic athetosis-like movements of the extremities; (2) rhythmic tremors similar to intention tremor and due to syphilitic injury of the midbrain, and (3) tic or clonus-like movements confined to the muscles of the face.

Hoff and Schilder assumed that in the spontaneous movements of tabes, it is necessary to have not only disturbances of deep sensibility but also injury of the central tonus apparatus. Taterka, however, has recently reported cases of tabes with spontaneous movements in which disturbances of deep sensation were lacking, and assumed that there was toxic injury of the striopallidum as a result of the syphilitic process. Recently, Schilder and Stengel have reported a case of athetosis-like movements in tabes. This patient had a lumbosacral tabes in which spontaneous movements occurred only in those limbs with disturbances of sensation, especially deep sensation. Necropsy revealed a typical tabes in the spinal cord and symmetrical areas of softening in the anterior portions of the pallidum. A careful study of the nervous system showed no other lesions besides those mentioned. Schilder and Stengel decided, therefore, that the loss of the centripetal impulses coming by way of the posterior columns was responsible for the athetosis-like movements, and the more or less confined process in the pallidum could not have produced the movements without the tabetic process. They state that "our case shows therefore the great significance of the loss of centripetal impulses for the occurrence of central spontaneous movements."

Stengel has attempted in this contribution to analyse these spontaneous movements. He studied 120 cases, 90 of them in tabetic patients, the rest consisting of multiple sclerosis, syringomyelia, Friedreich's disease and thalamus disease. "In the cases observed there was unquestionably a connection between pseudo-athetotic movements and sensory disturbance." In the 120 cases studied, none showed spontaneous movements in the absence of sensory disturbances, consisting of deep sensation losses chiefly, and of disturbances in position sense. In many of the cases there were also disturbances of deep sensation, but these Stengel minimizes, though stating that cases with disturbances of deep sensation alone are very rare. Stengel emphasizes that he wishes to make clear the relation of the spontaneous movements to the disturbances of deep sensation — position sense and movement sense chiefly. The first question which arises is the relation of

the spontaneous movements to the degree of sensory loss. Stengel has frequently seen cases with active movements and mild sensory disturbances, and cases with mild movements and severe deep sensation disturbances. He concludes, therefore, that a regular ratio between the degree of the spontaneous movements and the sensory disturbances does not exist.

These movements are most strongly present in: (1) certain cases of thalamus disease with sensory disturbances; these are not cases with true athetosis but of spontaneous movements with athetosis-like movements; (2) senile tabetic patients; (3) certain cases of tabes in which the deep sensation disturbances have advanced to a marked degree, and (4) certain cases of multiple sclerosis.

Spontaneous movements are more frequently seen in the upper than in the lower extremities because it is easier to examine the upper extremities. They are called forth by asking the patient to extend the arms, and are not present if the arms are supported. In cases in which besides the disturbance of deep sensation there is also a complete anesthesia of superficial sensation, these spontaneous movements do not occur. On the other hand, they are seen in cases in which the position and muscle sense are completely lost, contrary to the belief of Foerster. Stengel says that he has seen no case of disturbance of deep sensation in the upper extremities, in the presence of an intact motor apparatus, in which spontaneous movements were entirely lacking. In many cases they were only mild to be sure. On the other hand, under similar conditions they were often absent in the lower extremities. Stengel defines spontaneous movements as slow, involuntary movements involving the distal parts of the upper extremities in the presence of disturbances of position and muscle sense. They differ from true athetosis in the absence of the wormlike nature of the movements. Many cases show a slow spontaneous movement of the finger of the outstretched hand, in some cases affected by active or passive rotation of the head, and, though occurring in cases with hypotonia, the movements are accompanied by hypertonia. If, during the course of a movement, the finger is passively moved, it is found to be definitely spastic. Tendencies to pronation, deviation and abduction were often found in the arms, and in two cases of tabes Stengel observed tic-like movements of the face with distortion of the mouth, violent screwing together of the eyes and wrinkling of the forehead. Both cases had disturbances of deep sensation in the face. In many of the cases closing the eyes caused an increase in the extent and violence of the movement, and this has been assumed to be due to the fact that closing the eyes removed the optic control of the extremities. Foerster disagrees with this and states that looking at an extremity should control the movement. Stengel was unable to prove this in patients who could not control their movements by observing their extremities. If, on the other hand, they pressed their fingers firmly together they controlled the movements very easily. "Our observations contradict the fact therefore that in the intensification of spontaneous movements after closing the eyes, only the loss of optic control plays a rôle." If one takes a person with pseudo-athetotic spontaneous movements and places a sheet of paper before his eyes so that he cannot see his hands, the movements diminish or even cease. On the other hand, if he closes his eyes they increase. Whether the shutting off of light stimuli or the closing of the lids is the factor is not known. Stengel had an amaurotic tabetic patient who could not see, but who on closing his eyes experienced an increase of the movements. Another factor which also increases them is rotation of the head — active or passive.

In a small group of cases — presenile and senile tabes and multiple sclerosis — pseudo-athetotic movements of a particularly active type occur in the presence of insignificant sensory disturbances. The particularly active movements are explained by the fact that there is probably simultaneous involvement of the striopallidal system which is frequently implicated in the senile state. Stengel examined the basal ganglia in ten cases of tabes and found the usual degenerative changes described by Jakob, none of them of a specific nature. He concluded, therefore, that in a certain number of cases disease of the extrapyramidal system played a rôle in the production of pseudo-athetotic spontaneous movements. This

however, is only an additional factor, the first prerequisite being loss of centripetal impulses. Very active pseudo-athetotic movements have been described in: (1) cases of thalamus disease; (2) senile tabetic and tabetic patients with marked syphilitic disease of the extrapyramidal system, and (3) cases of multiple sclerosis. To these Stengel adds cases of tabes in nonsenile persons with marked sensory disturbances. These he believes are due to an indirect injury of the thalamus through injury of the centripetal tracts thereto. "Pseudo-athetotic movements arise as a result of direct or indirect injury of the thalamus." The present tendency is to look on chorea and athetosis as movements produced by the release of lower centers from higher control. Stengel says that this does not disagree with his belief. The loss of centripetal impulses leads to a disturbance of the central regulatory mechanism. Through disease of the posterior columns there is loss of many cerebellopetal and thalamopetal impulses. The territories into which the fibers of the dorsal column pass stand in the closest relation with the centers of the extrapyramidal system.

Certain cases of lumbosacral tabes in Stengel's series showed pseudo-athetotic movements in the upper extremities without sensory loss. This is explained by the suggestions that methods of sensory examination are still crude and that undoubtedly sensory disturbances existed but could not be detected.

ALPERS, Philadelphia.

THE PSYCHOPATHOLOGY OF ANXIETY. ERNEST JONES, Brit. J. M. Psychol. **9**:17 (May) 1929.

Morbid anxiety differs from fear in that the former term designates a state of mind and the latter an attitude to an object. Several features serve to make this distinction; in anxiety there is a disproportion between the external stimulus and the response, between the bodily and mental manifestations, and an internal disharmony among the manifestations themselves. In prefreudian days, morbid anxiety was thought to be due to an overexcitation of the nerve centers, either by normal stimuli acting on pathologically overexcitable centers, or by pathologic stimulation of normal centers. These views are irrelevant since "Freud discovered that it was not necessary to predicate either a pathological nervous system or pathological stimuli, for the evidence pointed unequivocally to the conclusion that the condition is induced by the action of normal physiological stimuli on a normal nervous system; all that could be called pathological were the social situations responsible for the form of stimulation."

From his studies on the anxiety neurosis, a condition which seems to occur whenever undue sexual excitation is combined with deficient opportunity for discharge, Freud was brought to lay "stress on the element of frustration which is common to all the situations in which it arises," so that the anxiety could be described as what was found in place of frustrated libido. He tried to explain the neurosis in terms of the chemical or physiologic components of libido. That is to say, he assumed that in sexual excitation certain chemical substances were generated or liberated and that when these could not be dissipated along their accustomed paths, anxiety arose. Anxiety was thus for Freud a substitute for libido, when this was frustrated, and was presumably developed out of it; to put it more accurately, the physiologic basis of anxiety was generated from the physiologic basis of libido, by some unknown process of chemical transformation.

In investigating the genesis of more complicated mental states such as the phobias, Freud found close parallels for the mechanism of his anxiety neurosis. Without going into the detailed structure of these conditions, one may say that they present the same picture of anxiety making its appearance as a substitute for a thwarted libidinal impulse. With his usual caution, however, Freud has refused to generalize from this observation, and does not maintain that all anxiety has this source, but only the morbid anxiety in the psychoneuroses. Until quite lately, he had always held the view not merely that this morbid anxiety arose in consequence of the repression of libido, but that it was actually derived from it

by some process of transformation, "perhaps akin to the transformations of energy with which we are familiar in the physical world."

The author always has disagreed with this view, and suggests that "morbid anxiety is a perverted manifestation of the fear instinct which, in the case of neurotic conflicts, has been stimulated to activity as a protection against the threatening libido." That is, in the course of the conflict between ego and libido the former responds by developing a reaction of fear. In his latest volume "Hemmung, Symptom und Angst" (1926), Freud has fully accepted this view and abandoned his previous more complicated one. The formula just reached gives an opportunity of contrasting morbid anxiety and normal fear. Morbid anxiety in the psychoneuroses is a defensive reaction of the ego against the claims of unrecognized libido, which it projects on to the outside world and treats as if it were an external object. But there appears to be an important difference between it and "real" dread, in that the latter concerns only the ego itself, arises only in connection with external danger to the ego, and has nothing to do with the desires of repressed libido. One is tempted to say that the real dread is a normal protective mechanism that has nothing to do with the abnormal mechanism of morbid anxiety. "Here, however, as elsewhere, the line between normality and abnormality is not so absolute as might appear." Real dread "can be dissected into three components, a mental state of fear and various activities suited to the occasion-flight, concealment, defence by fighting or even sometimes by attacking. On the affective side there is to begin with a state of anxious preparedness and watchfulness, with its sensorial attentiveness and its motor tension. This is clearly a useful mental state, but it often goes on further into a condition of developed dread or terror which is certainly the very reverse of usefulness, for it not only paralyses whatever action may be suitable, but even inhibits the functioning of the mind, so that the person cannot judge or decide what he ought best to do were he able to do it. The whole reaction of 'real' fear is thus seen to consist of two useful components and one useless one, and it is just this useless one that most resembles in all its phenomena the condition of morbid anxiety. Further, there is seen to be a complete lack of relation between development of dread and the degree of imminence of danger, nor does it bear any relation to the useful defensive activities. Thus, one does not flee because one is frightened, but because one perceives danger; in situations of extreme danger men very often respond with suitable measures of flight, fight, or what not, when they are not in the least degree frightened; on the other hand, the neurotic can be extremely frightened when there is no external danger whatever."

From his investigations of war shock, Jones agrees with Freud that the developed dread sometimes found in situations of real danger is a defense from the narcissistic part of the libido that is attached to the ego, for he found that "the only men who suffered from war shock were those whose libido, organized on a homosexual-narcissistic basis, was so attached to the ego as to become stimulated when the latter was threatened, i. e., in situations of real danger. This conclusion is fortified by considerations drawn from allied fields. In the more fully investigated cases of ordinary psychoneurosis, we know that anxiety arises in relation to over-development of a libidinal cathexis. Now the curious thing is that the latter can happen either from direct erotic excitation or from what might be called the opposite of this, namely, a threat to the libidinal organization." In the latter instance "a threat causes a libidinal investment at the point threatened, as though — to speak figuratively — the libido protects itself by increasing its strength. The fear reaction on the part of the ego is secondary to this increase." He recapitulates the steps in which he conceives the process to appear as follows: "First, perception of external danger. Secondly, normal fear response of mental alertness and physical preparedness (glycogenic stimulation, etc.). Thirdly, an over-investment of the ego with narcissistic libido as a protective response to the threatened danger. Fourthly, the evoking of 'developed' or morbid anxiety on the part of the ego as a response to the excess of narcissistic libido. This last response is obviously useless, and indeed detrimental, so far as the

external danger is concerned and consideration of it brings back to the question the precise relation of it to the internal 'danger' of excessive libido.

"Why is the (relative) excess of libido conceived of as a danger? It is evident that a person's libido, even in the adult sense, could be dangerous to his interests if uncontrolled. Behind this rational facade, however, much more remote and even more powerful mental forces are at work. It does not need much experience of neurotics to discover that their fears, even in the cases that appear to relate to current situations, are essentially of an infantile nature. When elucidated they are invariably shown to relate to various libidinal infantile situations, whether real or imaginary, and it becomes evident that this situation was in infancy, and still is in the unconscious, regarded as being absolutely intolerable. In face of it the child is helpless, alarmed and at the end of its resources. The erotic wishes exciting the child are impossible in the nature of things to gratify and it is this unrelieved need of gratification that is found intolerable. To put it more physiologically, the child has only a very limited capacity for enduring afferent excitation with no opportunity for any efferent discharge. The ultimate nature of the danger to the organism is that it may lose what even the ego itself does not want to lose, namely, the capacity for erotic gratification. It would appear that to the infant strong excitation without relief is tantamount to losing the very capacity for obtaining relief. I have suggested the term 'aphanisis' to denote this ultimate fate; the most familiar clinical manifestation of it is the castration complex. The group of reactions which later on will be called morbid anxiety have as their most striking feature the apparent lack of purpose and coordination in the manifestations. They must surely remind us of the very earliest reactions of the infant to distress of any kind.

"Freud has directed our attention to a still earlier situation in life from which many of the most characteristic features of anxiety would appear to be copied or perhaps even derived. That is, the event of birth itself."

PEARSON, Philadelphia.

THE NEUROLOGIC ASPECTS OF NASAL SINUS INFECTIONS: HEADACHES AND SYSTEMIC DISTURBANCES OF NASAL GANGLION ORIGIN. SIMON L. RUSKIN, Arch. Otolaryng. **10**:337 (Oct.) 1929.

Many symptoms attributed to toxic products are due to direct nerve irritation from the sinus membrane. There are direct influences on the nerve filaments supplying the sinuses and remote effects through pathways that appear impossible at first glance. The neurogenic disturbances may be classed under four headings: "(1) acute pains in sinus inflammation, (2) chronic neuralgias, (3) functional vasomotor and secretory states, and (4) systemic effects induced chiefly through the vegetative nervous system."

"The nerve tracts through which these influences are effected are the trigeminal system, the facial nerve system and the vegetative nerve system. The influence induced through the trigeminal system has received wide consideration, especially by Sluder, whose work is as classic as it is beautiful. I have tried to emphasize especially the symptomatology arising from the facial nerve and vegetative systems."

The nose in lower animals is probably the greatest factor in the preservation of the species. In the nasal mechanism the olfactory nerve probably does not play a more important rôle than the stimulation of the trigeminal, facial and vegetative systems. The animal scenting a change in environment reacts reflexly with its eyes and ears and its sympathetic and endocrine systems. Each of the three trigeminal structures has a ganglion process, possessing sensory, motor and sympathetic fibers. These act as reflex centers for rapid visceral reactions. All three are connected with each other and have direct connection with the vegetative nervous system. The author has seen sympathetic manifestations of fright induced by irritation of the sphenopalatine ganglion. He believes that nervous breakdowns, meaning usually a state of continuous fright, are frequent in cases of nasal sinus infections. In the nose is the only sympathetic nerve center superficially placed.

The customary neuralgic syndromes do not appear until years after the acute sinusitis. The roentgen examination reveals some thickening of the lining membrane but no evidence of fluid, as hyperplastic sinusitis. The author notes cases of ophthalmic neuralgia, maxillary neuralgia and trigeminal neuralgia immediately relieved by sphenopalatine ganglion treatments.

In a previous paper, he reported on trigeminal neuralgia and the excellent results obtained by injections into the nasal ganglion. In lower animals the facial nerve serves a greater rôle than in men. In fishes it takes over the function of the trigeminal system to some extent. "Here it plays prominently a sensory function. In the higher forms it is an integral part of the protective mechanism, innervating the muscles of the face in a manner to drive terror into its opponent. Especially significant is the action of the muscles surrounding the eyes, the action of the orbicularis oculi in narrowing the palpebral fissure, the corrugator supercillii in bringing the eyebrows together and the frontalis in bringing the eyebrows down in a menacing manner. The same muscles also constitute what are called the accessory muscles of accommodation; they are brought into play whenever the eyes are used intently and produce the expression of peering. The same mechanism works in accommodation. The interesting thing is that, in chronic irritation of the nasal mucosa with irritation of the facial nerve, the same mechanism is called into action as in the instance of stimulation of the nose in the lower animals in the search for food or detection of their enemies. As a result of the unnecessary overaction of these accessory muscles of accommodation, a distinct headache characterized frequently as "ocular headache" develops in these patients. Whereas the stimulation of the facial nerve mechanism in the lower animals by food or enemies is only temporary, that induced by disease processes in the nose is continuous and exhausts the patient physically and mentally. These patients have a frown characterized by a small vertical wrinkle at the head of each eyebrow. Observations on the eye are consistently negative and glasses produce practically no improvement. The eyes feel heavy, tired and uncomfortable. The pain across the back of the head, which the patients complain of, is caused by the pulling forward of the scalp by the frontalis muscle. These conditions frequently are encountered under the diagnosis of 'asthenopia.' In these cases, blockage of the nasal ganglion produces considerable relief. The overaction of the accessory muscles of accommodation relaxes, the eye is rested, and the patient has a feeling which is described 'as a feeling as though the eyes were washed.'

"I shall now go back to a careful consideration of the facial nerve. One usually thinks of the facial nerve as a motor system. The motor facial, however, travels with and is intimately associated with the nervus intermedius of Wrisberg, a sensory nerve that, according to Hunt, is the sensory portion of the facial nerve. The nervus intermedius, which I shall refer to as a sensory facial, has the geniculate ganglion which is situated on the motor facial nerve, where the motor facial makes its bend at the medial tympanic wall to run posteriorly toward the antrum of the mastoid, carrying with it branches from the sensory facial, which later leaves it as the chorda tympani. From the geniculate ganglion itself to the nasal (sphenopalatine) ganglion runs a fairly large nerve called the greater superficial petrosal."

It has been generally conceded that taste fibers pass by way of the greater superficial petrosal to the nasal ganglion. The author has relieved disturbances of taste and a burning sensation along the side of the mouth by blockage of the nasal ganglion with alcohol. He has diminished tear secretion by the same method. He calls attention to the fact that tear secretion is diminished on the side affected with Bell's palsy. He also calls attention to the fact that headaches in the back of the head may be due to disturbances of the facial nerve and that frontal half headaches are due to the trigeminal nerve. He states that pain in these different types varies. "The pains in the front half of the head are usually typical sensory pains of trigeminal origin; those in the back half of the head are myalgic, muscle pains. The sensation is that of stiffness and soreness, comparable to rheumatic pains." He has seen distinct myalgic nodes along the insertion of the cervical muscles and at the tip of the mastoid. The nodes are dissolved in a few minutes

after cocainization of the sphenopalatine ganglion, which acts on the facial nerve by way of the greater superficial petrosal nerve. Pain in the ear is relieved in the same way. Muscle pains are relieved through vasomotor action on the cranial autonomic system, and the pains in the neck, shoulders, arms and forearms, back and legs are relieved through the sympathetic system. A single application to the ganglion has relieved hiccups and sciatica. "Three or four treatments free a patient from such pains for a few years."

The pinching sensation at the root of the nose and discomfort of the face are due to the mechanism along the facial nerve. The symptoms of menopause are relieved by affecting the vasomotor apparatus through the nose. Conditions misdiagnosed as "globus hystericus" clear promptly after cocainization of the nasal ganglion through the cranial autonomic system. He supplements the nasal treatment with desiccated pituitary whole gland and calcium glycerophosphate.

Impaired hearing and tinnitus are caused in the same way by vasomotor disturbances and myalgic conditions of the stapedius muscle. The administration of a desiccated ovarian preparation has relieved itching of the ear. Pain from herpes zoster intercostalis is relieved by treatment of the nasal ganglion.

He classifies his cases as "anabolic" and "catabolic." He cites the case of a patient in a catabolic state, with a gain of 8 pounds, who was relieved from headaches and palpitation, following treatment of the sphenopalatine ganglion. He finds the patients in an anabolic state sensitive to cocainization and on this account advises the use of alypin solution. It is remarkable to observe how quickly the pain and nausea in these cases can be relieved by applications to the nasal ganglion; also spastic states in the gastro-intestinal canal, simulating gastric ulcer and cholecystitis. He has given instant relief from gastric pains in cases of supposed ulcer of the stomach, with one cocainization of the nasal ganglion. Patients with asthma have also been cured in this way. "Postnasal dropping" is due to the disturbed innervation of the mucus-secreting glands innervated through autonomic fibers to the nasal ganglion.

In the catabolic type, the disturbances are visceral and spastic; in the anabolic type, they are chiefly muscular, vasomotor and secretory. The author gives cases illustrating both types.

The endocrine system is also connected with the sphenopalatine ganglion. The pituitary gland is consistently influenced by nasal pathologic conditions. It is noted that in children sinusitis is more frequently seen in heavy set, overweight types with pasty complexions and puffy lower lids. He offers the suggestion that in these cases there may be stimulation of the pituitary gland.

HUNTER, Philadelphia.

CONSCIOUSNESS AS A PHYSIOLOGIC FUNCTION. JOHN AGERBERG, Acta psychiat. et neurol. **4**:103, 1929.

A.—The Concept of Consciousness.—In the strict sense of the word, consciousness implies an action. An action has a subject and an object. The subject of consciousness is the ego, the object anything that comes in contact with the ego; that is, consciousness is the reflection in the ego of objective reality. Consciousness cannot be imagined separate from objective contents any more than it can be imagined separate from the ego. This fundamental feature of metaphysical consciousness must be such that it is possible to rediscover it in the physiologic cerebral processes constituting the basis of consciousness. The physiologic process is in some way able to reproduce the phenomena which exist in objective reality. The whole content of consciousness must be the result of a combination between a number of ganglion cells and this is possible because of the almost infinite number of combinations possible. Consciousness can reproduce both concrete and abstract objects. In regard to the former, that which occurs in the cortex need be only a repetition of that which takes place in the sensory end-organs; i. e., consciousness in regard to concrete objects is simply an act of reproduction. It is more difficult to give a physiologic interpretation of the

reproduction in consciousness of abstract objects. It is hardly possible, however, to imagine anything abstract that has no connection with the concrete. Even the purely psychic processes cannot be imagined without an objective content. The first thought and first consciousness which arise in a child must have a concrete content and, therefore, the consciousness of the psychic process itself must be secondary to the consciousness of something concrete. The latter is a material act of reproduction in the cortex and it seems probable that the consciousness of a psychic process must correspond to a renewed reproduction—in another layer or part of the cortex. Ethical or esthetic values attached to concrete objects and all ideas of inner causal connection pertaining to the material world come into consciousness as the result of past psychic processes.

The ego has a place in consciousness also. A conscious ego cannot be imagined except in connection with a taking place of a psychic process, and in this connection assumes the position of the primary faction. Therefore, the physiologic correlation of the ego, consciousness, must also be primary in respect to the psychic process and the physiologic ego must be secondary to the concrete sensory impression. To express the matter more clearly, the conscious psychic processes are the result of impulses derived partly from the concrete external world and partly from something termed the ego. A natural explanation of the origin of ego consciousness has not been discovered.

B.—The Function of the Cerebral Cortex.—It may be assumed that consciousness is a specific function of the cortex and everything else that takes place in the body is unconscious unless it is reflected in the cortex. The purely biologic importance of the cortex, the organ of consciousness, in relation to the bodily organism as a whole is displayed clearly in the phylogenetic development of the former. From all points of view, the neo-encephalon is regarded as a reaction system of a higher order than is the paleo-encephalon. In regard to the relation between these two systems it is evident that the functions pertaining to the cortex constitute an addition to an already existing and complete reaction system corresponding approximately to the stage of development in fishes, and that this animal reaction system even in the case of man has not lost any of its original importance. In regard to the functional relation between the cortex and the remainder of the brain, those animals possessing only a paleo-encephalon are reflexive machines—entirely dependent on the concrete situation—while man by means of his consciousness, i. e., neo-encephalon, is able to keep himself in contact with situation factors which are not concretely present either in time or in space. Man reacts to his consciousness picture, the lower vertebrates to the sensory impression of the moment.

C.—The Consciousness Picture.—The course of the higher forms of reaction connected with consciousness is mainly determined by two factors: (1) the forming of the consciousness picture and (2) the material mode of reaction respecting this picture. Referring to the theory of consciousness, three kinds can be distinguished: (1) an object consciousness; (2) an ego consciousness, and (3) a consciousness of psychic processes. The first is composed of sensory impressions of the moment and preexisting recollections; the latter is arranged in a more or less orderly manner in respect to one another. The internal picture must be so accurate a reproduction of the external world that time and space are correctly combined in it. Concrete experience is supplemented by ideas and imaginations so that experiences are arranged as a single universal combination—an actual world picture. A direct sensory impression also meets with the same double relationship to experience and conceptions. From a pure experience point of view it will be only the sensory impression which will enter consciousness, but from the conception point of view it will be the imagination of the object. Although in point of time the sensory impression comes first, it falls on ganglion cells of the cortex already full of previously formed pictures; it must so to speak smuggle itself into the picture which is at that moment present in consciousness. The first thing which awakens consciousness is the relation borne by the external impulse to the already conscious connection and it is not until afterward that the impression

itself becomes conscious. A sensory impression may influence the idea picture without itself entering consciousness.

The ego constitutes a source of internal impulses which in combination with outer impulses sets the conscious psychic processes going. It seems entirely spontaneous—the expression of a special inherent activity of the cortex. It is logically necessary that a natural cause must exist behind the apparently spontaneous one and as the connection cannot be displayed in consciousness it must be related to some unconscious process. As the cortex is connected with the paleoencephalon systems the impulses arising in that system, being unable to result in object consciousness, must make their presence known in consciousness and be perceived as internal spontaneous impulses. However, these impulses are not spontaneous. Voluntary movement consists of three phases, only one of which is conscious: (1) a preconscious phase during which the impulse from the sensory receptus travels to the brain; (2) a conscious phase during which a definite object is set for a motor act; (3) a postconscious phase in which a number of acts are carried forward automatically by which the end in view is obtained. The ego consciousness which appears to arise spontaneously may follow a preconscious phase of varying duration. The sensory impulses that form the sensory limb of the reflex arc really arise within the body and are integrated and distributed to the cortex by the thalamus, as is the case also with impulses entering the body through the sense organs. In accordance with this view, the whole of the content of consciousness must be connected with a preconscious spontaneous interest or, in neurophysiologic language, all the processes in the cortex are connected with processes in the encephalon and most immediately in the thalamus. Even as regards the apparently purely associative trains of thought it is probable that the association takes place through the thalamus.

The spontaneous ego in consciousness is nothing more than the personal organism, itself unconscious, with its various vital processes and vital needs, the impulses of which travel by the vegetative nervous system to the thalamus. The thalamus, because of its connections not only with the vegetative nervous system and sense organs but with the whole cortex and the automatic motor centers, the last two connections being each reciprocal, is the main integrating organ of the body. As a result, an impulse entering the cortex probably will consist of a combination of external and internal sensory impulses and those coming from the cortex and the automatic centers. The associative course in the act of thinking may be only an oscillation of impulses between the cortex and the thalamus.

Each actual consciousness picture, then, is the synthesis by the thalamus of impulses which are partly conscious and partly unconscious. This is true whether the consciousness picture has the character of a sensory impression, a memory picture or an abstract conception.

PEARSON, Philadelphia.

THE PSYCHOLOGIST'S INTEREST IN HEARING. MADISON BENTLEY, Arch. Otolaryng. **10**:282 (Sept.) 1929.

As knowledge of the processes involved in hearing increases, one becomes less dogmatic in explaining the mechanism of hearing. The physicist, the embryologist, the neurologist, the pathologist and the psychologist find it impossible to interpret their observations in the light of the Helmholtz theory. The psychologist's interest lies in the living organism, being especially set on the experience of hearing sounds. He is concerned only with what the organism hears and how it hears. The otologist is interested in the disturbance of hearing from the pathologic and involutional processes and for its relief. "Let us ask the psychologist at once how he approaches his experience of hearing and how he proposes to use the knowledge of physics, physiology, neurology and the rest to advance his problems.

"The matters pertaining especially to the psychologist may be considered under four main headings: (1) a description of the simpler auditory experiences; (2) the relation of these experiences to the forms of energy delivered to the cochlea; (3) the relation of them also to aural structures and mechanisms, and (4) an

account of various more complex auditory phenomena (combination tones, intermediate tones, beats, fusions, consonance, the octave quality, binaural synergies and special localization).

The Simpler Auditory Experiences.—"What are the simpler sounds? From the psychologist's point of view, no real headway can be made until it is known what sounds are; by 'sounds' are meant what the organism actually hears and not physical vibration. Consequently, one begins as simply as possible by interrogating the organism as to what, in plain terms, it experiences when it uses its ears. One good reason for beginning with the simpler sounds is that the ear is an analyzing apparatus which distinguishes (with certain limitations) the components of a complex wave-train delivered at the tympanum. The facts here are difficult and the descriptive account is not complete. It is found that one class of sounds may be identified as tonal, but that these sounds differ in various ways among themselves and are not simply loud and weak pitches to be strung on a colorless string or represented by a straight line. Among the rest of the sounds can be distinguished a class of noises, which have thus far resisted all attempts to order and to classify but which stand related in significant ways to some, at least, of the tones. Besides the tones and the noises one seems to discover intermediate sounds represented by certain constituents of the voice and of musical instruments. These intermediate sounds, sometimes called formants, are at once tonelike and noiselike. It appears that the aural functions cannot be properly understood until more is known about them. Helmholtz dismissed them as harmonic combinations of tones, but Hermann and others have shown that they are not so readily to be disposed of (as, for example, in the vowel sounds).

"Coming back to the tones, it appears that these sounds — no matter how simply they are taken — are not to be exhausted by the epithets 'high' and 'low,' 'weak' and 'strong.' Among the other characteristics of them stand volume and brightness and perhaps vocality, tonality and tonal color."

Volume suggests a quasi-spatial attribute. The one is not only grave and the other high, but the one is huge, massive and voluminous, the other small, fine and compact.

"Brightness, again, inheres in tones, increasing from below upward as the vibrational frequency is increased. High tones are also bright, and low tones dull. The first lucid description of this characteristic seems to belong to the physicist Mach, who possessed the knack — rare among physicists — of distinguishing what he heard and saw from the conceptual description of radiant and molecular energies, i. e., of distinguishing the experience itself from the stimulating agent acting on the receptor. It is easier to identify the brightness aspect of tones than it is to relate it exactly to the other attributes. A convenient way to observe brightness is by means of the siren disk with concentric rings. An air jet passed through the radial holes in these rings as the disk revolves acquires the same frequency of pulse and, therefore, gives a common pitch, no matter where the ring stands on the disk. The sounds, however, differ notably in brightness and in dulness. This difference is probably independent of volume and loudness. Since these differences in brightness have been supposed to depend on the time ratio of disk aperture to intervening surface (and, therefore, to the form of wave-train), I was surprised to discover that they remain when the disk is replaced by simple radial sectors which presumably do not disturb the wave-train as the jet moves from the center to the periphery of the rotating mass. The relation of brightness to pitch and volume has been investigated by a determination of its difference limen (or rate of change) with change of frequency. One observer found that the difference limen for brightness roughly coincides with that for pitch and so concluded that they are different names for one and the same attributes. These observations, however, need checking. The difference limen for volume has been observed to be much larger than that for pitch, but nothing like a complete survey for either volume or brightness has yet been made for the entire tonal series. The term tonality suggests the musical relations of the tone to its octave. These tones are alleged to be more alike in a certain respect than either is like its immediate neighbors above

and below. Vocality refers to the resemblance of tones to the vowel sounds. Good observers have found the vowels recurring in a regular order as tones pass from low to high. Other good observers have thought that the vocal character is not inherent in the simple tone. The plain fact is that the tone, although simple, presents so many qualitative shadings and so many sides and aspects that its adequate description is extremely difficult. Another decade may be required to clear up this descriptive account. Meanwhile, a regard for the facts does not permit a return to the old Helmholtzian simplicity and the older rigid parallelism of pitch with rates of frequency and of loudness with amplitude.

"This matter of tonal character may seem to otologists to be merely an academic refinement without any real issue or importance, but that is not so. Until one knows the character of the simpler sounds, one can relate the sound itself neither to the physical properties of the stimulus nor to the structures and functions of the ear. A great deal hangs on the establishment of these triangular relationships. Without them one cannot interpret the comparative morphology of the fishes, amphibia, reptiles and birds, forms in which the sense of hearing was being elaborated. Neither can the anatomy and the physiology of the ear be understood, nor can one diagnose and treat all disorders of the hearing mechanism."

Noises possess pitch. They differ with respect to both brightness and volume which may or may not prove to be identical with the same properties of tone. In pitch, noises probably run neither so low nor so high as tones. The theories of hearing give many varying and conflicting views, and after these were cleared up one could not be sure of an adequate doctrine of hearing. One of the most extraordinary accomplishments of the aural functions is the nice account which they take of spatial direction or localization. There seems to be evidence here of a central synergy which coordinates the separate functions of the two disparate ears. Some of this may be tactual sense. To prove this the author advises study of cases lacking in one tympanic membrane, and the malleus and incus might also be trained to compare diotic sounds. He states that his understanding of audition is in the stage of revisable but working hypotheses. The author describes analysis of sound by the combination of sound and frequency and the principle of shifting maximal response. Any theory of aural functioning will have to deal with the troublesome fact of refractory period. Analogies recently found in the vacuum tube have helped in the understanding of these additional tones.

The author then discusses the inconsistency of the Helmholtz theory in the light of modern studies. Eventually, the knowledge of anatomy, physiology and psychology will become sufficient to integrate all of these theories.

This is an excellent article but should be read in the original.

HUNTER, Philadelphia.

ATYPICAL RETROBULBAR NEURITIS IN TUMORS OF THE CRANIAL BASE. G. WEILL and J. NORDMANN, Rev. d'oto-neuro-opht. **7**:1 (Jan.) 1929.

Through collaboration of neurologists, otorhinologists and radiologists, knowledge of retrobulbar neuritis is becoming more exact. Generally, two forms are recognized, having in common a diminution of vision with persistence of a central scotoma and without modification of the eyegrounds. In the first form, described by Graefe in 1866, there is sudden, almost total, loss of vision with a central scotoma; it occurs in young subjects, usually female; it is unilateral and there is sensitiveness to pressure on the globe or with lateral movements of the eye. In the majority of the cases it is an early and often sole symptom of disseminated sclerosis. The second is a chronic form, due to chronic intoxication by alcohol, nicotine, lead or carbon bisulphide; it is bilateral from the beginning, progresses slowly and never causes such a pronounced loss of vision.

Besides these two typical forms, there are a number of intermediary and atypical forms of varied etiology. These are the ones which have caused confusion. They have a different evolution, although at certain periods they can be confounded with either the acute or the chronic forms. In order to throw light on these atypical forms, the authors report three cases, well studied, of tumor at the base.

They recognize that tumor is not the sole cause of this condition; other lesions, such as inflammation of the posterior group of nasal accessory sinuses, may be causative.

CASE 1.—The patient, aged 25, with unimportant family and past history, had had good vision in both eyes and had used the right eye in aiming. In December, 1927, he noticed that he could not see the center of a target well. In April, 1928, he noticed rapid loss of vision in the right eye.

A general examination and Bordet-Wassermann tests gave negative results. On May 26, there was an absolute central scotoma of the right eye; the peripheral limits were normal; chromatic sense was almost completely abolished; only movements of the hand before the eye were seen. The globe and fundus were normal; the pupil reacted well to light and in accommodation. The left eye was normal. Nose and throat, neurologic and dental examinations gave negative results. Vision diminished to 5/50 by July 12; the central scotoma was replaced by a paracentral scotoma on the temporal side; the peripheral limits of the visual field contracted. On August 9, the right papilla was white; there was temporal hemianopia and vision was reduced to perception of fingers at 20 cm.; in the left eye the papilla was hyperemic; the vessels were full and tortuous but the papilla was not projecting; vision was 5/5; the visual field showed a supertemporal notch and a temporal hemiachromatopsia. These conditions warranted a diagnosis of a disease in the region of the chiasm, which was confirmed by roentgenograms: invasion of the floor of the sella turcica, which was widened, with flattening of the sphenoidal sinus. The retinal arterial tension was normal. Lumbar puncture revealed: pressure normal; some traces of albumin; no cells; Bordet-Wassermann reaction negative; Queckenstedt test negative.

The right eye became absolutely blind. In the left eye, the hemiachromatopsia was transformed into almost complete hemianopia, but with no hemiopic reaction of the pupil.

Roentgenotherapy was used without benefit.

CASE 2.—The patient, aged 39, whose father had been a drinker, four years previously had suffered from a cerebral concussion from trauma. There had been no abuse of alcohol or tobacco. The illness began on May 1, 1927, with violent headaches and lowering of vision in the left eye. Following an epistaxis and purulent discharge from the nose, loss of vision, which had been proceeding slowly, progressed rapidly.

Examination on Sept. 10, 1928, revealed: ocular motility perfect; right eye normal, vision 5/10; left eye, fundus normal, vision, ability to count fingers at 1 meter; glasses did not improve the vision. Tonus and retinal arterial tension were normal. With an ordinary perimeter the visual field showed in the right eye an absolute paracentral scotoma on the temporal side and a temporal retraction for colors. The peripheral limits were normal. In the left eye there was a large absolute central scotoma. Neurologic and dental examinations gave negative results. The Bordet-Wassermann reaction was negative. A purulent sinusitis of the left maxillary antrum was present. Visual fields taken with Bjerrum's curtain showed: right eye, hemianopic scotoma; left eye, central scotoma and a peripheral retraction. A roentgenogram showed an extensive osseous tumor in the region of the sella and sphenoidal sinus.

In spite of the duration of more than a year, the left disk was normal. The diagnosis was made by the use of Bjerrum's curtain in outlining the visual fields, which showed a temporal hemianopic scotoma of the right eye. The hypophyseal tumor was first manifested by an atypical unilateral retrobulbar neuritis. The left-sided sinusitis had no causal relation.

CASE 3.—The patient, aged 52, had had diabetes for two years. Vision in the left eye began to fail rapidly and in three weeks the eye was almost blind (atrophy of the left nerve). The right eye was normal; vision was 5/8, and the visual field was normal. Four weeks later, blindness existed in the right eye. This was a case of retrobulbar neuritis followed by atrophy.

The patient was admitted to the hospital on Oct. 7, 1928, in profound diabetic coma. There was simple atrophy of both disks; there was marked exophthalmus on the right, which was easily reducible. A pansinusitis was present. A roentgenogram showed extended osseous lesions in the region of the sella, with destruction of the base of the anterior fossa and floor of the sella. The patient died on October 24.

At autopsy there was found a tumor of the base invading the right frontal lobe which contained a large empty abscess cavity communicating with the nasal sinuses; the cribriform plate, the roofs of the orbits and the sella were destroyed. The tumor formed the base of an abscess cavity. The nature of the growth was a stratified pavement epithelioma, of basal cell type, arising from the sinuses.

Atypical retrobulbar neuritis is often the first sign of a tumor of the base of the skull. Roentgenography of the base of the skull is demanded in all cases of retrobulbar neuritis and must be repeated unless a considerable amelioration occurs rapidly or if the etiology remains obscure.

DENNIS, Colorado Springs, Colo.

STRUCTURE OF THE ARTERIES OF THE BRAIN AND CHANGES WITH INCREASING AGE. W. M. HACKEL, Virchows Arch. f. path. Anat. **266**:630, 1928.

The structure of the arteries of the brain is of especial interest in relation to the amount, the arrangement and the localization of the elastic tissue of the intima. These all change as age progresses and it is difficult to make a distinction between the normal and the pathologic events in the wall of the vessel. The men who have worked on this problem especially have all been interested in the splitting up of the elastic layer of the brain arteries into two or more laminae and look on this as an especial characteristic of the brain. Nonne and Luce give a general description of the structure of the brain arteries of different calibers and look on the splitting up of the elastica interna as characteristic of arteriosclerosis and syphilis. Binswanger and Schaxel carried on studies concerning the structure of the arteries of the brain in the new-born infant and in persons of various ages between 30 and 40 and 50 and 60, and concluded that in the brain of the new-born infant there is a well developed architecture which with later growth changes in its proportions and its arrangements. The especial growth of the elastin takes place about the fortieth year and begins in the intima; later on in the media. The atrophy of the layers of the muscularis begins at about the sixtieth year. The connective tissue shows the greatest tendency to increase wherever there is elastic or muscular tissue. Thoma emphasized the special structure of the arteries of the brain in the presence of a double lamina elastica interna, a normal media and a thin adventitia that contains connective tissue and a small number of elastic fibers.

Hackel examined thirteen patients of ages varying from 15 days to 50 years. He divided these, after making microscopic studies of the arteries, into three groups.

Group I comprised patients from the age of 15 days to 12 months. In these the lamina elastica interna was well developed in the larger arteries. Immediately beneath this was a layer which stained weakly, and below this was a layer which stained well. The intima was usually found in marked waves and the elastic tissue in it was usually distributed in one distinct layer, although there were occasional places where the layer was split. Beneath this lay the thin muscular coat which stained well and was sharply defined. In the larger arteries there were occasional thickenings of the intima at the places where small branches were given off. In these thickenings the elastic layer was often split. In the small arteries, however, there were no places where there was any thickening or splitting of the elastic layer.

Group II, which contained cases of patients between the ages of 6 and 13 years, showed the splitting of the lamina elastica interna with great regularity in the larger arteries. As in group I, this was more marked where branches

were given off. The thickening of the elastic layers was usually associated with a thinning of the other layers. In the small arteries the elastic layer was always thicker than in the other group and it also stained more deeply. The media and adventitia showed occasional thickening, but there was no great difference between these and those of group I.

Group III contains all persons between the ages of 20 and 50 years. In all there was a very marked splitting of the elastic membrane. This occurred not only in the larger arteries but also in the small branches. In these it was usually only a separation into two layers, while in the larger arteries the lamina elastica interna was often split up into three. The third layer appeared to come off from the subendothelial layer, and in between these elastic laminae there were often small broken up elastic fibers which looked like specks. Besides this increase of elastin in the intima there was also an increase in the amount of collagen. In the media and in the adventitia there was no change from the appearance found in the other groups.

On the ground of these observations one can conclude that the structure of the walls of the arteries of the brain changes with increasing age. All the brain arteries are designed on the type of "muscular arteries," but they differ from the regular muscular type in that they have a thick lamina elastica interna which in the larger arteries is obvious before there is any splitting up. There is also beneath this elastic layer a more weakly staining interstitial substance and two more darkly staining layers bordering this. A structure like this has been described in other arteries. Furthermore, the arteries of the brain are unique in the absence of the lamina elastica externa and in having only a weakly developed adventitia. As the age of the person advances, there is an increase in the splitting up of the elastica. This begins even in childhood and is at first localized in the larger arteries, especially where they give off their branches. As age advances, this increases gradually and begins to be found in the smaller arteries as well as in the larger ones. In old age this process becomes very conspicuous. The splitting up of the lamina elastica is first recognized by the differentiation in the staining of the thick inner subendothelial layer and an outer thin but more darkly staining layer.

COBB, Boston.

TUBERCULOMA OF THE CEREBELLAR HEMISPHERE WITH PONTOCEREBELLAR SYMPTOMATOLOGY. HENRI ROGER, M. BRÉMOND and P. SIMÉON, Rev. d'oto-neuro-opht. **7**:26 (Jan.) 1929.

André Thomas said with reference to cerebellar tumors, "There are few affections whose symptomatology is as varied and as disconcerting." The authors previously had presented a case of voluminous tumor of the acoustic nerve with the cerebellar symptomatology accentuated. In this report they present a case of tuberculoma of the cerebellum with signs pointing to an acoustic tumor.

A chauffeur, aged 22, gave a history of occipital headaches for ten months, and vertigo for eight months. Headache, at first bilateral, soon became localized on the right and was relieved temporarily by acetylsalicylic acid. The first attack of vertigo occurred on getting out of bed and caused falling; there had been no falling since, but there was a sensation of swaying to the left which had been more frequent during the past three months. Transient visual obnubilations occurred at frequent intervals. The patient had continued to drive and had never had an accident. Vomiting accompanied the headache and vertigo only twice. Only two other symptoms were elicited: seven months previously, paresthesia of the face (forehead excluded) and right half of the tongue had lasted for ten days and there had been continuous tinnitus, bilateral but predominating on the right; it varied in intensity and was relieved by pressure on the neck. The past history was without significance except for a transient otorrhea in childhood and pleurisy at 18.

On examination, there was no pain on percussion of the skull. There was absence of ocular paralysis; vision was normal on the left, 1/10 on the right;

there was bilateral papillary stasis, which was worse on the left. Sensibility of the fifth nerve was normal, but the right corneal reflex was diminished. Hearing was equal on the two sides. Vestibular tests showed: slight inclination of the body to the right on standing; slight deviation of the right foot inward on pointing, but the right hand pointed correctly; with the arms extended there was elevation of the right hand. In walking with closed eyes, the patient deviated to the right and after five or six goings and comings, his position was completely reversed. Nystagmus to the left occurred after turning and was of normal duration. There were no dysmetria, adiadokokinesis or deviation in walking. With the dynamometer, the reading was 41 on the left and 36 on the right; the patient was left handed.

He soon became worse, vomited every three or four days, and had more headaches and vertigo; there was an increase of the papillary stasis; vision in the right eye became almost nil. The spinal fluid showed: tension increased; leukocytes 1.2; albumin 0.30. The Bordet-Wassermann reaction was negative both in the fluid and in the blood.

The localization was assigned to the right cerebellar fossa because of the right occipital headache; tinnitus in the right ear; the absence of deafness; swaying to the right; deviation to the right in the Babinski-Weill test; nystagmus; hypoexcitability of the right labyrinth; Bárány's sign normal in the arms, abnormal in the legs; transient paresthesia of the face and right half of the tongue; abolition of the right corneal reflex. The precocity and intensity of the signs of trouble in the right labyrinth pointed to a cerebellopontile angle lesion. The slight and delayed accentuation of the cerebellar syndrome suggested a progressive pressure of extracerebellar rather than intracerebellar origin. A troublesome sign was the left (opposite) facial paresis, but the authors have seen this in a tumor of the acoustic nerve.

Operation: A wide exposure was made of the cerebellar fossa. The patient died when the bone flap was raised. The meninges were tense and not pulsating; there was more resistance on the right on palpation.

Autopsy: The right lobe of the cerebellum was increased in size; the bulb and pons were pushed to the left. A tumor, the size of a large nut, was present in the external half of the right hemisphere. The left temporal lobe was depressed and grooved by the compressed left half of the cerebellum. The ventricles were dilated. The tumor was a caseating tuberculoma.

Comment: The error in diagnosis might have been avoided if cochlear symptoms had been more carefully considered: there was no deafness, which is an early and constant symptom of an acoustic tumor. A peculiar sign was that at times in the terminal period the patient had violent pain in the right side of the head with vertigo and pallor, accompanied by immediate cessation of the tinnitus for a short time. When the latter reappeared the pain and vertigo disappeared. (Pressing on the neck likewise relieved the tinnitus.) Probably this was due to a vascular spasm or to a sudden increase of intracranial tension.

DENNIS, Colorado Springs, Colo.

THE PATHOGENESIS OF LIPODYSTROPHY. E. K. EWSEROWA, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:489 (Feb. 11) 1929.

In 1911, Simmonds described under the name of lipodystrophy a disease characterized by atrophy of the subcutaneous fatty tissue in the face, arms and upper part of the trunk, with simultaneous involvement of the fat in the gluteal region and the lateral parts of the hips. His case occurred in a girl, aged 11, and ran a very slow course. In 1926, Gangliomo collected sixty such cases from the literature, all in women and all with slow courses. The disease may occur in men and may begin late, as Long and Bickel have shown. There is an atypical form in which the fat atrophy involves either only the upper part of the trunk, the face and hands, or is accompanied by a hypertrophy of the fat in the gluteal region. Barraquer, in 1906, described the first variant, five years before Simmonds,

and in 1912 Laignel-Lavastine described a case with fat hypertrophy of the lower extremities without atrophy. Simmonds regarded these merely as variants of the lipodystrophy which he described. Progressive lipodystrophy may be accompanied by symptoms of vegetative and endocrine insufficiency — trophic disturbances of the skin and nails, pigmentation of the skin, hypertrichosis, dryness of the hair, tendency to sweating attacks, acrocyanosis, polyuria, oliguria and glycosemia.

The pathogenesis of the disease is not clear. Simmonds first classed it with the trophoneuroses and in a later communication denied the possibility of a pure sympathetic origin on the basis of a lack of other sympathetic signs; he compared the disease to progressive muscular atrophy. Other authors believe that the disease is either an endocrinogenic disease, or of neurogenic or mixed origin. A small group look on the disease as of tuberculous or toxic origin. Aplasia of the thyroid has been found in a few cases, but feeding thyroid has always resulted in an increase in the fat atrophy. Hypertrophy and hyperplasia of the ovaries have been found. In a few cases atrophy of the suprarenals has been found, and also hypertrophy and hyperplasia of the hypophysis. In a case of lipodystrophy, Marburg investigated carefully all the endocrine glands and the tuber cinereum and found regressive changes in the ovaries and hyperplasia of the hypophysis.

Lipodystrophies are observed in lesions of the peripheral nervous system, spinal cord and brain. Peripheral type: Fatty atrophy has been observed in guinea-pigs after section of the sciatic nerve, and Landouzy has seen it in man in sciatica. Others have found it in alcoholic polyneuritis. Giese found a laminated sort of fatty atrophy in a case of hereditary syphilis following the course of the lumbar roots. Spinal type: Müller removed the lower part of the cord in dogs in order to study the localization of the bladder and rectum functions, and observed, as an accidental thing, a fatty hypertrophy of the lower extremities. He also reported a fatty disease of the legs after a contusion of the spine, and in a second case after a fracture of a lumbar vertebra. Simmonds observed a unilateral fatty hypertrophy of the tongue as a result of an abiotrophy of the hypoglossus which was confirmed histologically. He also found a disappearance of fat in one mamma after an infantile poliomyelitis. Cerebral type: Unilateral fatty hypertrophy and atrophy in hemiplegia are well known. Allied to these is hemiatrophia facialis in which the sympathetic plays an important rôle, and which differs from lipodystrophy through participation of the skin and joints in the process.

Ewserowa reports a case of lipodystrophy in a woman, aged 33, who at 30 began to have attacks of migraine in the left side of the head. A few months later, the left side of the face was definitely atrophied, the menses became irregular, severe and painful, and the atrophy spread to the upper part of her arms and trunk. For a year she had had jacksonian epilepsy in the left hand; it had now spread to the face and was accompanied by loss of consciousness. Physically, she showed hyperreflexia, lost corneal reflex, dysesthesia of the left trigeminal distribution, and lipodystrophy of the Barroquer type — fatty atrophy of the face, upper extremities and upper part of the trunk. Roentgen examination showed a bony tumor of the sella turcica, but without visual field changes.

The case of Ewserowa differs from the classic cases of lipodystrophy in the late onset, the rapid development in the course of three years and its accompaniment by other cerebral symptoms. Ewserowa subscribes to the cerebral genesis of lipodystrophy on the basis of the case reported.

ALPERS, Philadelphia.

ANXIETY STATES. J. A. HADFIELD, Brit. J. M. Psychol. **9**:33 (May) 1929.

After citing the various organic theories — toxemias, endocrine disturbances (and pointing out the danger of regarding the endocrine disturbances that accompany anxiety as the cause, when they are more probably the result) — which have been evolved to explain anxiety states and the reasons why these do not seem tenable, Hadfield alines himself with those who hold the theory of psychologic causation. He agrees with Jones (The Psychopathology of Anxiety, *Brit. J. M. Psychol.*

4:17, 1929, abstracted in this issue of the ARCHIVES, p. 1049) on many points, but disagrees with him on two.

"The first concerns the nature of anxiety as against normal fear. Dr. Jones remarks that, as compared with normal states of fear, in morbid anxiety the bodily manifestations are excessive. But surely the difference is not in the exaggeration of bodily states as such, but in the nature of the bodily manifestations. Any emotion like fear normally expresses itself in bodily activities, but activities of a voluntary and purposeful type, such as running away. If for any reason, whether external, like the impossibility of escape, or from internal inhibitions, like moral scruples, this tendency to the voluntary expression of fear is thwarted or suppressed, the energy appears to be dammed back and expresses itself in over-activity of the autonomic nervous system, giving rise to anxiety. It is natural to suppose, therefore, that anxiety is much more likely to occur when there is already over-excitation of the nervous system, as in toxaemia, and toxaemic conditions may therefore be a very important predisposing factor in the production of anxiety states.

"The difference then between normal fear and anxiety does not lie in the excess of bodily movements as such, but in the damming back of the normal expression of fear, so that it fails to express itself in normal activity and discharges itself in activities in the organism itself connected with the autonomic nervous system.

"The second is a difference with Dr. Jones' paper of fundamental importance and concerns the aetiology of morbid anxiety."

The author does not believe that "the sexual feelings are not the only ones which threaten the ego. Fear in childhood, leading to chronic anxiety later, may arise from the lack of protection and security; it may also arise from its own aggressive impulses. In the actual origin of these abnormal fears and dreads there is one circumstance which obtrudes itself with extraordinary constancy, namely, the occurrence of some marked cause of fear in infantile life, especially infantile illnesses, feelings of suffocation, brutal treatment from a cruel nurse, starvation, isolation, difficulties in birth, and other causes. These may not in themselves cause anxiety states, but we regard them as the very factors which predispose to later attacks of fear, and the dread produced in them is reproduced in the later attacks of anxiety. Anxiety states are infantile reactions, for when an individual is afraid of the dark, of loneliness, of space, he is merely reverting back to infantile forms of behavior.

"When situations of abnormal fear occur in infancy, then a conditioned reflex is set up, and situations in later life reminiscent of this tend to call forth the exaggerated responses of infantile life in the form of overwhelming dread which we meet with in our patients. Pavlov has shown that a conditioned reflex of fear in dogs tends to persist as a neurosis, and it is not surprising that experiences of this kind occurring in infancy, when the mind is so susceptible, the brain so plastic, and the emotional life so overwhelming, leave their mark on the whole life. A child who has such experiences naturally regards the world as a dreadful place, and reacts accordingly. Its reactions are of two kinds, egoistic self-assertiveness, and a tendency to seek protection by being amenable, suggestible and moral. These are the typical character traits of the patient suffering from anxiety and it is the threat to these — the patient's sense of power or moral sense which precipitates the anxiety in later life." PEARSON, Philadelphia.

PARANOIA: ANALYSIS OF A CASE. RUTH MACK BRUNSWICK, J. Nerv. & Ment. Dis. **70**:155 (Aug.) 1929.

A woman, aged 30, was analyzed over a period of two and a half months for violent jealousy of her husband, delusions of his infidelity and illicit intercourse with her stepmother, sexual frigidity, threats and attempts at suicide. The mother had died when the patient was 3, and she grew up with an older sister, Louise, feebleminded and hypererotic, who later became a prostitute and developed demen-

tia paralytica. The greatest enemy, she felt, was her stepmother; the next her mother-in-law, with whom she and her husband had to share one bedroom. Her dreams indicate an erotic attachment to the sister Louise with whom, as early as the age of 3, she had engaged in mutual masturbation, with a considerable sense of guilt. She was relieved of the fear of masturbation, but later developed the delusion that the analyst was about to commit her to a hospital for the insane. The next revelation is known as a "penis envy," which shows itself in frequent dreams recalling actual childhood sex experiences. In comparing herself with her brother as a child, she had come to believe that her own genital had been cut off. She recalled admiration of her sister's pubic hair because of the genital it was supposed to conceal. Both sisters were known in the neighborhood as bed-wetters. After the sister became a prostitute, the patient became jealous of the men who took her away from her. During the analysis she developed several paranoid episodes, in the first of which she suspected the analyst of removing her husband's affection; in the second, the negative transference developed, with a desire for the analyst's death and marked irritation and the feeling that the analyst suspected her of theft; the final episode consisted of death threats against the analyst, representing her sister, and hallucinations of laughter. Hatred of the husband for the possession of a penis became gradually converted to an acceptance of his superior potency as the dream material revealed early repressed sex experiences with her older sister. During the period of negative transference there was a better sexual adjustment to the husband as well as a cessation of satisfaction from masturbation. The hatred of the stepmother became explained by identification with the neglectful sister who became the object of the patient's homosexual jealousy.

Most of the dreams in this case are barely distorted reproductions of the past. There was no evidence of intellectual impairment or emotional deterioration in this case, and the patient's work was never seriously affected by the analysis or the psychosis. There was also some justification for some of the patient's delusions in that the two older women, the stepmother and the mother-in-law, tried to influence the husband against her. Moreover, the author found no evidence of regression in this case as in most cases of paranoia, but sufficient evidence of fixation on the sister Louise, of whom the husband is seen as the successor. Nothing in her experience had prepared her for coitus, and she was unable to transfer her homosexual love of the sister to the husband until after the analysis. The brevity of the analysis is explained chiefly by the transformation of the psychosis into a transference psychosis, and by the patient's ability to master the ensuing transferences. A feature of the case is the absence of the Oedipus complex; this is explained as a pre-Oedipal level of fixation. The homosexuality is not the usual one based on love of and identification with the father (the active masculine homosexuality), but appears to be based on the normal passivity of the small child to the phallic woman represented by her sister. Since the analysis, two years of complete mental health, despite a serious mastoid operation, have occurred, and the patient is said to be happily extroverted and adjusted to her family and husband.

HART, Greenwich, Conn.

WEBER'S SYNDROME WITH VERTICAL PARALYSIS OF THE EYE. H. SCHAEFFER and OUMANSKY, Rev. d'oto-neuro-opht. **7**:96 (Feb.) 1929.

A woman, aged 48, was seen on Oct. 6, 1928, with the syndrome of Weber which had appeared two days previously. Nothing of importance was noted in the family or the past history. One healthy child was living and there had been no miscarriages. In July, she had had headache, diminution of vision, muscae volitantes, hypo-acusis, slight tinnitus and vertigo, but she improved after one month in the hospital. In October, she had had transient diplopia and drooping of the left lid, followed by paralysis of the left motor oculi; on the next day, icterus and right hemiplegia developed, although she was not completely unconscious.

On examination, the patient responded to questions and repeated phrases without sense. She had incontinence and a right hemiplegia, which included the face. The exit of the right facial nerve was tender. There was complete paralysis of the left third nerve. The left eye was closed and the globe was carried outward; the eye could not be moved inward, upward or downward. The pupil was dilated; the right reflex was lost. The tendon and abdominal reflexes were abolished on the right. Babinski's sign was positive on the right. Movements of the left arm were maladroit, trembling and athetoid. A general examination gave negative results.

Spinal puncture yielded fluid showing: cells, 2.2; albumin, 0.2 Gm. The Wassermann reaction was negative in the fluid and in the blood. Hypodermic injections of cyanide of mercury caused prompt amelioration in four days, though the hemiplegia and oculomotor paralysis remained.

There was now a vertical paralysis of vision in the right eye. Voluntary and automatic movements of the globe were diminished and there was complete paralysis of the elevators. There was no nystagmus. The right pupil responded to light. One month later, rapid improvement was noted. The vertical paralysis of vision was better. The paralysis of the elevators persisted for voluntary movements, but when the gaze was fixed on a point and the head flexed the eye turned up. Thus the synergistic movements of the head and eye caused a contraction of the elevators which the patient could not bring about through the will.

Comment.—In a woman with unsuspected and untreated syphilis, there appeared a Weber syndrome, characterized by a right hemiplegia with disturbance of the third left cranial nerve and a paralysis of the elevators of the right eye. In the beginning, paralysis of the eye muscles involved both voluntary and automatic movements. Later, movement of the depressors and automatic movement of the eye upward were reestablished while voluntary elevation remained impossible. The Weber's syndrome indicates a lesion of the foot of the left cerebral peduncle, involving the pyramidal fibers and roots of the oculomotor nerve; to a certain degree the lesion involves also the upper segment of the peduncle, which explains the disturbance of sensibility, trembling, athetoid movements and static disturbances. It is not illogical to assume that the lesion affects also the interoptic association fibers in the quadrigeminal region. It is not necessary to assume a cortical lesion to explain the dissociation paralysis of the elevators with loss of voluntary movement and conservation of automatic action.

This case confirms the opinion of Parinaud that absence of elevation of the ocular globe is a paretic phenomenon, and disproves that of Alajouanine that dissociated paralyses of function are a consequence of disturbances of tonus and are not paralyses. To explain the modification of the vertical paralysis, one may note that in consequence of antisyphilitic treatment, the synergistic automatic movements, which are earlier integrated than the voluntary movements, reappeared first.

DENNIS, Colorado Springs, Colo.

OPIUM ADDICTION. A. B. LIGHT, E. G. TORRANCE and OTHERS, Arch. Int. Med. **43**:206 (Feb.), 326 (March), 556 (April), 684 (May), 878 (June) 1929; **44**:1 (July), 194 (Aug.), 376 (Sept.), 693 (Nov.), 862 and 870 (Dec.) 1929.

After a study of opium addicts in the narcotic wards of the Philadelphia Hospital, Light and his colleagues conclude that the drug addict is not intrinsically deteriorated, at least not so far as his organic constitution goes. It follows from this, they believe, that could the addict be freed from his craving there would be no physical bar to complete rehabilitation. They were unable to discover the physiologic or pathologic basis for the withdrawal symptoms, which symptoms they list in order of frequency as yawning, lacrimation, sneezing, restlessness, sweating, hot flashes, diarrhea, cramps and others less common. These symptoms last about three days when they gradually disappear, but early introduction of the drug will clear them up. There are certain characteristics of the withdrawal period, however, such as the

response to tests of physical fitness (Schneider's tests were used) which were not improved by readministration of morphine. After two weeks of abstinence from the drug, the addict seems to lose his tolerance, and in such cases the former addict who resumes his customary large dose is apt to die or suffer from toxic effects. Except for a slight leukocytosis (9,000 per cubic millimeter), the addict shows little variation from the normal in his cardiorespiratory apparatus or blood chemistry. Studies of the functions of the viscera did not reveal any constant change. It is true that anemia and emaciation are common among drug addicts, but it is believed by the authors that the unhygienic surroundings and methods of living are adequate to account for this. A negative water balance was noted during the withdrawal stage in most of the subjects. The use of scopolamine in doses ascending from $\frac{1}{200}$ to $\frac{1}{100}$ grain (0.00032 to 0.00065 Gm.), every four hours for nine doses, was reported, and no changes except some loss in weight (average, 7 pounds [3.2 Kg.]) and rise in temperature (average, 1 degree F) were noted. Slight leukocytosis and slight albuminuria were often found after treatment with scopolamine. Intravenous injection of morphine demonstrated the speed with which the drug was removed from the blood stream. Urinalysis disclosed that about 9 per cent of the daily intake of morphine is eliminated by way of the kidneys. Small and inconstant proportions of the intake were discharged in the fecal matter. The subjects of the special papers appearing in the *Archives of Internal Medicine* during 1929 were: February: types of addicts, and technic of study; March: physical fitness of addicts; April: cardiorespiratory studies; May: blood chemistry of addicts; June: miscellaneous observations on organ function of addicts; July: withdrawal symptoms; August: treatment with scopolamine; September: injections of morphine into blood stream; November: excretion of morphine; December: water balance. This series of papers does not offer any suggestions as to the practical management of the drug addiction problem, but presents a series of carefully recorded observations as to the physical characteristics of the addicts. The most important of the conclusions drawn from this work is the demonstration of the physical parity of the addict and the normal man, extending the hope that relief from the craving for the drug will be accompanied by a general return to normal status.

DAVIDSON, Philadelphia.

FOCAL ATROPHY OF THE BRAIN (PICK'S DISEASE). M. S. KAPLINSKY, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:670 (Feb. 20) 1929.

Since Pick's description of the interesting disease which bears his name, twenty cases of a similar nature have been reported. Much still remains to be determined. Kaplinsky reports a case in a woman, aged 62, who gradually, in the course of five or six years, developed increasing dementia and aphasic disturbances. The patient lacked a number of words and expressions in her speech. She was often unable to find the word for an object the significance of which was clear to her, and the name of which she recognized when it was spoken. She was able to give the significance of many objects without being able to name them. She could state that a match was for smoking, and a comb for combing the hair, but could not name the objects. She could repeat the names of objects without, however, realizing their significance. She often spoke autochthonously and it was impossible to quiet her. Kaplinsky describes the aphasia as a transcortical sensory aphasia, and believes that the focal lesion lies in the temporal lobe in his case.

The differential diagnosis of Pick's disease is difficult. In Kaplinsky's case syphilis was ruled out readily by the course of the disease, the absence of somatic-neurologic symptoms and the negative serology. Arteriosclerosis was more difficult to dispose of, but the absence of nervous symptoms, such as irritability, vertigo or paresis, after a course of several years seemed to rule this out also. The general clinical picture and the age of the patient denied a diagnosis of senile dementia. A senile dementia of six or seven years' standing would undoubtedly produce a mental disintegration with tendency to confabulations, disturbances in

consciousness, disorientation and delirious phenomena. Alzheimer's disease was ruled out because it begins earlier and develops to a deep degree, without such sharp focal signs as in this case. Only one possibility remains for the case described: Pick's disease. All the characteristics which are a part of this disease are present — mental deterioration and focal symptoms, which usually are speech disturbances. The development of the speech difficulties are of interest. Kaplinsky points out that human speech has developed its complexity from generation to generation of development, and in the individual person develops from simplicity to great complexity, from a cry to the spoken word. In the case which he reports the speech process so carefully built up was gradually lost. From the beginning of the illness the patient went gradually from the complicated sentence and speech, year by year and month by month, to a simpler one, until she gradually lost speech which became poor and primitive. This demonstrates that the process was biologically regressive, and step by step removed all that the patient had built up in years and which man had developed during centuries. As always in these cases, the process involved the younger areas of the brain. Spatz has pointed out that in Pick's atrophy it is the portions of the temporal and frontal areas which are most involved.

The etiology of Pick's atrophy is doubtful. Pick looked on his cases as atypical examples of senile dementia. However, senile plaques have never been found in cases of Pick's atrophy, nor are the fibrillary changes of Alzheimer ever seen. Later writers, such as Altmann, Richter, Gans and Quari and Spatz, look on the disease as a heredodegeneration.

ALPERS, Philadelphia.

PARTIAL SYNDROME OF THE SPHENOIDAL FISSURE WITH EDEMATOUS PAPILLITIS. J. NORDMANN and O. METZGER, Rev. d'oto-neuro-opht. **7**:102 (Feb.) 1929.

On Aug. 3, 1928, a man, aged 28, entered the clinic complaining of headaches of gradually increasing intensity, which began in 1926 but had been less severe for the past year. They were continuous and were worse at night. He had diplopia on looking to the right and there had been hypesthesia of the right half of the forehead for the past month. The patient smoked and drank beer moderately; he said that he had not had venereal infection. He suffered from a slight shock during the war and had influenza in 1919. In 1921, he had a fall which rendered him unconscious for ten minutes but he was able to resume work on the following day.

On examination, vision, visual fields and color vision were found normal; the right papilla was congested but not elevated; the veins were dilated; there was paralysis of the right external rectus. The left eye was normal. Arterial tension was normal in both eyes. The right corneal reflex was as lively as the left but its sensitivity was less. There was slight superficial hypesthesia in the distribution of the ophthalmic branch of the right fifth nerve, and the circles of Weber were enlarged. The vestibular apparatus was normal, and there was no evidence of cerebellar or pyramidal disturbance. The Bordet-Wassermann reaction was negative in the blood and spinal fluid.

On August 28, there was a distinct choking of 3 diopters of the right disk with a small hemorrhage. Vision was 5/15, and was not improved by glasses.

Antisyphilitic treatment (Quinby) was begun, and after twelve injections of quinine bismuth iodide and twelve injections of cyanide of mercury, the vision was found normal, the choking in the right eye had disappeared and headaches had ceased, but the paralysis of the right sixth nerve remained. The patient still complained of pain in the right parietal region and over the exit of the right infra-orbital nerve.

In spite of the negative Wassermann reaction, antisyphilitic treatment was used with complete success. One should not neglect the therapeutic test even in the face of its absence.

As to localization, the involvement of the fifth and sixth nerves, with edematous inflammatory papillitis, suggests a syndrome of the apex of the orbit from a syphilitic osteoperiostitis. In general, two syndromes of the apex of the orbit are

recognized: One involves a greater or less number of motor and sensory nerves and as all these traverse the sphenoidal fissure it is logical to locate the lesion there. In the second syndrome, the optic nerve is also involved. To explain this (the syndrome of Rollet) one must postulate a more extended lesion involving the optic foramen. Usually the disease of the optic nerve is a simple atrophy from pressure without vascular changes.

Cases of orbital apex syndrome with papillitis are more rare and are explained by an extension of inflammation to the optic nerve.

In the case reported, the lesions of the nerves were relatively discrete and their regression was rapid. Only a few nerves were affected and one assumes that the lesion in the sphenoidal fissure was small. The integrity of the third nerve warrants the assumption that the inflammation did not extend to the optic foramen. The picture cannot be explained by one lesion; it is believed that the original lesion was at the sphenoidal fissure, causing sensory and motor paralysis, and that a secondary one caused the papillitis.

DENNIS, Colorado Springs, Colo.

CERTAIN PERSONALITY PROBLEMS IN RELATION TO MENTAL ILLNESS, WITH SPECIAL REFERENCE TO SUICIDE AND HOMICIDE. R. G. GORDON, Brit. J. M. Psychol. **9**:60 (May) 1929.

The author attempts to formulate an answer to the following questions: (1) Are suicide and homicide unrelated, or are they different aspects of the same tendency? (2) Is there any justification for the coroner's verdict "suicide while of unsound mind"? (3) May any ordinary person commit suicide or homicide? (4) Does the psychoneurotic person ever commit suicide or become insane?

He considers that man is a social being and, further, a consciously universal being who has a tendency to adjust himself to the general processes whereby the universe seems to be governed and evolved. So far as a man is adjusted to these processes, and is in the swim of evolutionary progress, so will suicide and homicide be increasingly difficult — suicide, because it represents a denial and shirking of the duty of the individual as an integral part of the universal whole; homicide, because it represents a disregard of the rights of other members of the universal whole. Suicide and homicide are therefore related, both representing failures in adjustment at this high level of adaptation. There is a difference in personalities in relation to this point of adaptation to the progressive evolution of the social environment. A certain proportion of human beings are definitely set toward this adaptation to universal harmony, so that they are observed to be urged in the direction of adjustment in their general behavior. This would seem to make suicide and homicide impossible for them. This type of person, when confronted by a situation which he cannot meet, breaks down in a psychoneurosis. However poor his performance may be, the neurotic person does have a strong fundamental set toward adjustment. His real conflict, of the true meaning of which he is unconscious, is so much worse than the illness that the continuance of the latter is inevitable. If the set toward adjustment is then inherently a strong one, suicide is impossible. Although the neurotic person may play with the idea and perhaps accomplish it by accident, he never commits suicide. In many cases which are diagnosed as neurosis the patients do commit suicide, but if suicide occurs the diagnosis is wrong.

The second type of personality does not enjoy this set toward harmony and readily turns away from an adjustment to the universe. When this person is confronted by a situation that he cannot meet, he breaks down into a psychosis. Such a person cannot change effectively under the ordinary psychotherapy since he has no inherent impulse to do so. His environment must be changed to suit him. Suicide or homicide is always a possibility.

Suicides and homicides belong to a definite type of personality, potentially psychotic, although the suicidal or homicidal act may be the first overt manifestation of this potentiality. Gordon sums up his argument as follows: (1) Suicide and homicide are closely related and both represent a failure in the personal

adjustment to the social environment, the universe and reality. (2) The coroner's jury, except in very exceptional cases, is correct in the verdict of "suicide while of unsound mind." (3) The apparently ordinary person may under special circumstances commit suicide or homicide if of the potentially psychotic type, and (4) not if he is of the potentially psychoneurotic type, for such people do not commit suicide or homicide or become insane.

PEARSON, Philadelphia.

TRIGEMINAL NEURALGIA AS AN INITIAL SYMPTOM OF MULTIPLE SCLEROSIS. E. HERMAN, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:773 (Feb.) 1929.

In contrast to the motor disturbances, sensory symptoms are less frequent in multiple sclerosis. Such symptoms as formication, burning sensations and cold flashes are the most frequent and characteristic of the early sensory disturbances in multiple sclerosis. Pains are the least common of these disturbances. They may have an arthritic character localized chiefly in the joints, or may be tabiform in nature (shooting, boring, wandering pains); or they may be myalgic and caused by severe muscle contractions, radicular or finally girdle pains. Foix, Lévy and Schiff-Wertheimer stated that there are patients with multiple sclerosis, who have long standing headaches accompanied by vomiting, and so imitate a brain tumor. In one case the pains lasted for six months before the nature of the disease became evident. French authors speak, therefore, of a "forme céphalalgique de la sclérose en plaques." The pain phenomena may actually dominate the clinical picture as in "sclerosis multiplex dolorosa." These pains may be typically neuralgic in nature, so that sciatica may often be observed as one of the first symptoms.

Cases of trigeminal neuralgia, either in the beginning of or during the course of multiple sclerosis, are rare. Guillain observed it in only two cases, and it has been mentioned by relatively few — Oppenheim, Berger, Marburg and Parker. Oppenheim described a case in which trigeminal neuralgia was the first and longest lasting symptom. At necropsy, a sclerotic focus was found at the point of exit of the trigeminal nerve. Parker reported four cases. At necropsy one of these showed a sclerotic focus at the point of entrance of the trigeminal nerve into the pons, with smaller foci in the lower part of the medulla in the spinal portion of the nerve. Parker stated that trigeminal neuralgia in multiple sclerosis is rare.

Herman reports a case in a man, aged 40, who for seven years suffered from pain in the right side of the face, localized above and below the orbit and in the jaw. These pains were so intense as to preclude eating or speaking during their occurrence. They were intermittent and increased during eating and speaking. For three years he had had a weakness in the lower extremities, developing into a stiffness. Physically, he showed a slight nystagmus, a slight weakness of the right masseter, a marked peripheral facial paresis on the right side and a spasticity of the lower extremities without sensory changes. The abdominal reflexes were lost; the patellar reflexes were increased, and there was a bilateral Babinski sign. The pains in the face persisted after injections of alcohol, but disappeared with roentgen therapy.

ALPERS, Philadelphia.

THE HEMATO-ENCEPHALITIC BARRIER IN EXPERIMENTAL TRYPANOSOMIASIS. G. P. ROSENHOLTZ, Med-biol. j. **6**:135, 1928.

Dogs and rabbits were infected with *Trypanosoma equiperdum, Doflein* and the hemato-encephalitic barrier was studied in the various stages of the disease. The permeability was studied by Stern's method. A 3 per cent solution of trypan blue (5 cc. per kilogram of body weight) was introduced into the jugular vein. Ten minutes afterward, a solution of sodium ferricyanide (5 per cent) and sodium iodide (3 per cent) was injected into the vein, using 10 cc. per kilogram of body weight. Twenty minutes after the first injection, the animal was bled and cerebrospinal fluid was obtained by means of a cistern puncture. The iodide was determined colorimetrically. The ferric cyanide was reduced to prussian blue, while the trypan

blue was determined by the color of the spinal fluid as well as by histologic examination of various parts of the brain.

In dogs, as a result of the infection, the permeability was definitely lowered, as evidenced by the presence in the fluid of crystalloids as well as the occasional appearance of the colloid — trypan blue — outside the cerebral vessels, that is, in the tissues of the brain. This does not take place in healthy animals. The permeability was increased only with the appearance of the trypanosome in the peripheral circulation. This phenomenon took place, however, even when the dog was free from fever. There was no relationship between the various stages of the infection and the degree of increased permeability. There is a certain individual variation in the resistance to the various crystalloids.

In the case of rabbits, it is interesting to note that the infection, from the very beginning, takes a mild, chronic course. The animals did not appear sick, although thirty or forty days afterward, examination of the spleen showed the presence of trypanosomes. As far as the barrier is concerned, the results were identical with those in dogs, i. e., the permeability was increased and the barrier lowered. It is interesting to note that the introduction of trypan blue caused death of the rabbits within half an hour. This gives some clue to a better understanding of the pathology of sudden death in parasitic infections, which were previously ascribed to anaphylaxis.

In all these experiments controls were made by using healthy dogs and rabbits.

KASANIN, Boston.

SPONTANEOUS NYSTAGMUS. I. SOMMER and J. C. YASKIN, Arch. Ophth. **2**:57 (July) 1929.

Nystagmus represents a defense reaction of the muscles of the eyeball consequent on difficulties in fixation. There are three types of nystagmus, ocular, neurologic and otologic. In an investigation of the special characteristics of these types, Yaskin and Sommer suggest a simple method for differentiating one from the other. They consider in order: (1) type, (2) direction, (3) degree, (4) frequency and amplitude, (5) association, (6) permanence and (7) associated clinical data. The type, if pure, is suggestive of a neurologic or an ocular form of nystagmus, whereas a mixed type, such as horizontal rotary, is commonly associated with the otologic variety. If directed to one side this is of little diagnostic value, but if undulating (undirected) it suggests an ocular nystagmus. Neurologic nystagmus tends to have its quick component directed to the side of the lesion of the stem, whereas in otologic nystagmus the quick component is often toward the healthy ear. By degree, Yaskin and Sommer mean the direction to which the eye must be turned to bring about the nystagmus; in the first degree, the eye turns in the direction of its quick component to bring out the tremor; in the second degree, it develops on looking straight ahead, and in the third degree, the tremor occurs when the eye is in the direction of its slow component. The diagnostic value of this is that in third degree nystagmus the variety is neurologic or otic, whereas in second degree nystagmus it is probably ocular. The frequency and amplitude tend to be medium in labyrinthine nystagmus and extreme (slow or fast) in ocular cases. Nystagmus that is not simultaneous in both eyes is always ocular. Permanency is also suggestive of ocular nystagmus, whereas changeability indicates a neurologic type. In addition to this examination, which should be adequate to uncover the type of nystagmus, the associated clinical data should be considered; that is, otologic, ophthalmologic and neurologic examinations should be conducted as indicated. The authors then consider diplopia occurring during nystagmus, suggesting that if there are no oculomotor palsies to account for this complication the diplopia is probably of central nervous system origin. The paper is concluded with the presentation of a case of nystagmus of mixed origin, two cases of otologic nystagmus, three of neurologic type and four of the ocular type.

DAVIDSON, Philadelphia.

DIAGNOSTIC DIFFICULTIES IN OTITIC PERIPHERAL FACIAL PARALYSIS. A. SARGNON and P. BERTEIN, Rev. d'oto-neuro-opht. **7**:18 (Jan.) 1929.

The ideas of Gellé as to the otitic origin of facial paralysis have been generally accepted by neurologists up to a few years ago. But now the search for the cause is no more limited to an otoscopic and functional examination of the ear. The authors show the difficulty of determining the otitic nature of paralysis and criticize two symptoms which are not always indicative of inflammation of the tympanum, viz., redness of the drum membrane and pain in the ear. Gellé showed that inflammation from the tube attacked first the inner wall of the tympanum, in the upper part of which the facial nerve runs, and it is only later that the drum membrane becomes injected. Furthermore, it is not the suppurative cases that most often are complicated by facial paralysis. The authors think that this discrete redness of the membrane does not always indicate infection of the tympanum. Two other factors can cause the redness: infection of the geniculate ganglion and a vasomotor disease independent of microbic invasion.

Inflammatory tumefaction of the geniculate ganglion is capable of causing paralysis and at the same time can cause infection of the mucosa of the tympanum by way of a possible dehiscence in its bony canal. The paralysis is more often due to zona than to an acute otitis media, the latter being secondary. The vasomotor system of the tympanum is highly developed and its susceptibility is great. Thus the membrane and tympanum can become hyperemic and the nerve can suffer compression from the tumefied mucosa. Exposure to cold can cause paralysis by producing circulatory disturbances.

Attention is called to the intimate connection of the facial with the sympathetic, between the nuclei of the fifth and seventh nerves and the anastomosis between their terminal fibers. Otalgia in facial paralysis is not always a sign of tympanic inflammation. The facial contains sensory fibers and it also possesses a sensibility borrowed from anastomosis with the fifth nerve, hence the painful radiations in the temple in painful facial paralysis. The possibility of inflammation of both sensory and motor roots (meningoneuritis) in facial paralysis, syphilis being the chief cause, is also mentioned.

Three illustrative case histories are given.

DENNIS, Colorado Springs, Colo.

NISSL AND THE THEORETICAL BRAIN ANATOMY. H. SPATZ, Arch. f. Psychiat. **87**:100 (April) 1929.

In this number of the *Archiv für Psychiatrie und Nervenkrankheiten,* which contains a series of addresses delivered at the fiftieth anniversary of the foundation of the Psychiatric Clinic at Heidelberg, Spatz discusses the contributions made by Nissl to the study of neuro-anatomy. The first and probably most important contribution was the demonstration of the cell structure by means of the method which has since been known under his name. The studies which Nissl has made of the structure of the nerve cell by the aid of this method have radically changed the direction of investigation in neuro-anatomy. It has thrown into the limelight this important component of the structure of the brain and turned the interest of investigators in that field away from the previously used methods of Golgi and others. From the beginning, Nissl appreciated the fact that one had no means of telling whether in the picture presented by his method one was dealing with conditions that were actually present in vivo. Nevertheless, it was important as a relative or as he called it "equivalent" value. This meant that one was in a position to determine the pathologic influences on the tissues by comparing the condition of a given component in brains of persons normal before their death with that of persons who were sick.

Starting from this point, Nissl's program was to attempt to find a correlation between clinical entities and changes in the cell structure as demonstrated by this method. In this respect, he was disappointed, as even to date no such definite correlations have been discovered. His histologic studies along this line, in human postmortem material as well as in experimental animals, yielded a large number

of instructive data but failed in discovering a definite correlation. Spatz next discusses Nissl's investigations in the later years of his life, viz., those on the "specific nerve tissue" and the predilection of diseases for certain cortical layers. In both of these fields, Nissl started investigations which are still being continued, and although the original idea was eventually molded and reshaped as new data were discovered, it still finds expression in the work, for instance, of the Spanish school on the microglia and of Vogt on the selective pathology of the brain.

MALAMUD, Iowa City.

THE VEGETATIVE CENTERS IN THE MIDBRAIN. B. SCHWABAUER, Med.-biol. j. **6**:140, 1928.

The author reviews critically the experimental work of the past few years and questions the generally accepted opinion that the corpus striatum is the regulatory center of the vegetative nervous system, while the various nuclei in the corpora mamillaria and the tuber cinereum control the specific functions of the vegetative nervous system, such as the regulation of heat, the carbohydrate metabolism, etc. If this is correct, the removal of the organs which these nuclei control ought to result in degenerative changes in the nuclei themselves. Extreme care ought to be exercised before drawing any conclusions, such as variation in stains and the individual equation, in accepting the criteria of degeneration and variations within the range of normal. The only significant pathology is the change in form and shape of the cell, as well as changes in the chromatin granules.

Several series of experiments were performed on dogs. In the first series, one of the kidneys was removed and the dogs were killed in from one to three months afterward. As this was inadequate to show any definite changes, in other dogs the kidney, the spleen and one lobe of the liver were extirpated in various combinations. Histologic examination of the midbrain and medulla showed slight changes in the thalamus, striatum, nucleus of the vagus and substantia gelatinosa Rolandi. The changes consisted in alterations in the form and shape of the cells.

In another series of experiments, the vagus and sympathetic were cut on one side. The dogs were killed three weeks afterward. There were definite degenerative changes in the medulla, striatum and thalamus, but very little change in the corpora mamillaria or the tuber cinereum.

As a result of these experiments the author thinks that nuclei of the corpora mamillaria and the tuber cinereum are not the only relay stations for the impulses of the vegetative nervous system going from the subcortical centers. Most of the tracts leading from the subcortical centers are relayed in the striatum, thalamus, corpus Luysii and the red nucleus. The functional interrelationships of the various parts of the brain are extremely complicated and no simple scheme, such as is available at present, can do justice to the actual function of the central nervous system.

KASANIN, Boston.

PERSONALITY CHANGES IN CHILDREN FOLLOWING CEREBRAL TRAUMA. J. KASANIN, J. Nerv. & Ment. Dis. **69**:385 (April) 1929.

The author finds that in 10 per cent of cases of the Judge Baker Foundation in which the conditions were diagnosed as psychopathic personalities the patients had had serious injury to the brain during childhood or adolescence, with either fracture of the skull or severe concussion of the brain. A control group of 120 cases not showing psychopathic tendencies showed only 2 cases of serious injury of the brain. Following Trotter, he regards the three important characteristics of concussion as: instantaneous onset, loss of consciousness and circulatory failure. Trotter found headaches, giddiness, tinnitus, memory defects and slight changes in disposition as signs of incomplete recovery from such concussion. Cannon's discovery that a brain deprived of its blood supply will take up water from a solution isotonic with the blood, thus causing further swelling, may be applied to swelling which occurs after severe cerebral concussion observed at autopsy.

Pierce Bailey, in 1903, reported irritable, boisterous, uncontrollable behavior in children after cerebral injury. Adolf Meyer, in the same year, showed instances of fatigue, retardation of thought, impaired memory, irritability, headaches and extreme susceptibility to alcohol in adults from the same cause.

The author presents fifteen cases in some detail of children with personality changes following trauma. Thirteen of these were regarded as psychopathic, having first been treated as functional cases with prolonged and unavailing psychotherapy and social study. He is of the opinion that severe injury of the brain interferes with the formation of the proper inhibitory influences in the integration of the child's personality. Encephalography by the lumbar route should be used more extensively in the study of these cases. When psychotherapy fails, persons should receive prolonged and intensive training in correctional institutions under intelligent supervision. The outlook is more favorable than in the behavior disorders subsequent to encephalitis.

HART, New York.

DRUNKENNESS: A QUANTITATIVE STUDY OF ACUTE ALCOHOLIC INTOXICATION. EMIL BOGEN, Am. J. M. Sc. **176**:153 (Aug.) 1928.

The alcoholic concentration of the urine, breath or body tissues constitutes the most reliable single factor in arriving at a correct diagnosis of the degree of acute alcoholic intoxication of a patient. The author analyzed 500 cases suspected as acute alcoholic intoxication, using as a clinical criterion of intoxication the decree of the higher courts of Ohio, in the case of Gard versus State (33 Ohio Circuit Courts, 632), in which it was specifically stated that besides an alcoholic breath, a flushed face and a disposition to talk loudly and freely, it must be shown further that he had "lost either the control of the faculties . . . . or of the muscles of locomotion."

For ascertaining the concentration of alcohol in the urine, blood, spinal fluid or other tissues, 1 cc. of the specimen, which had been kept previously in an icebox, was placed in a test tube and a purified current of air was bubbled through it at a moderate rate and then passed through 5 cc. of the reagent mixture of one third of 1 per cent potassium bichromate in 50 per cent sulphuric acid for ten minutes, both tubes being immersed in a boiling water bath. The concentration of alcohol in the breath and spinal fluid showed a close agreement with that in the urine.

A rather convincing series showed the specific correlation in the severity of the symptoms with the quantity of alcohol in the urine. Patients could be divided into five main groups according to the amount of alcohol in milligrams per cubic centimeter of urine. In group 1, with from 0 to 1 mg. of alcohol there was not a single intoxicated patient, but 40 per cent had an alcoholic breath. In group 2, showing from 1 to 2 mg. of alcohol, more than one-half the number of patients were intoxicated, although more than 80 per cent had an alcoholic breath, dilated pupils and flushed face. In group 3, which showed from 2 to 3 mg. of alcohol, there was an increase in nearly all the symptoms of alcoholic intoxication. In group 4, with from 3 to 4 mg. of alcohol, almost all of the patients were intoxicated, and only 3 per cent were able to stand without marked swaying. In group 5, having 4 mg. of alcohol and over, all the patients were in a state of actual alcoholic unconsciousness.

MICHAELS, Detroit.

THE HAEMATOPOIETIC FUNCTIONS IN GENERAL PARESIS. H. WILFRED EDDISON, J. Ment. Sc. **75**:242 (April) 1929.

The author studied post mortem the bone-marrow from the ribs and lymphatic tissue from various situations in cases of dementia paralytica in which no treatment had been given that would have been likely to stimulate hematopoietic functions. He also studied the blood of fifty persons who were in various stages of dementia paralytica before treatment and of thirty of these persons during and after treatment with relapsing fever. From these observations he drew the fol-

lowing conclusions: Impairment of function of the leukoblastic tissues with diminution of the leukocytic reserve occurs in dementia paralytica and is not observed in nonparetic syphilis. These changes may account for the ready occurrence of bed sores and intercurrent infections. Induced infection that causes a polymorphocytosis results in the appearance of large numbers of immature leukocytes in the blood. The degree of such reaction varies inversely with the stage of the paretic disease. The better the general condition of the patient after pyrexial treatment, the more normal is the differential leukocyte count; the converse is equally true. The progress of dementia paralytica can sometimes be delayed by measures that cause increased leukogenesis; on the other hand, these measures tend to hasten the progress of the disease when they produce an unfavorable leukocytic response. When pyrexial therapy of a leukogenic type is contemplated, a preliminary test should be carried out to eliminate cases that show a poor leukocytic response.

SINGER, Chicago.

THE EFFECTS OF THE SEPARATION OF THE MEDULLA AND SPINAL CORD FROM THE CEREBRAL MECHANISM BY THE EXTIRPATION OF THE EMBRYONIC MESENCEPHALON. J. S. NICHOLAS, J. Exper. Zool. **55**:1 (Jan. 13) 1930.

Operations were performed on embryos of *Amblystoma punctatum* before the stage of motility was attained. Extirpation of the mesencephalon had no effect on the cell proliferations which occur in the first five segments of the spinal cord. Dominance of the medulla in this connection is thus shown by implication. Limb and pronephric rudiments, transplanted into the wound, acted as a landmark and as a block to union of the cut ends of the nervous system. The pronephric tubules, because of rapid growth, produced pressure within the developing brain case. This was sufficient to alter the growth of the basal portions of the skull and to cause pressure changes in the surrounding nervous system. The intrinsic growth of the cerebral hemispheres was sufficient to produce new vesicles in connection with the original hemispheres when these were restricted in their developmental relations. The limb transplanted to the head region grew well, and although its innervation was sometimes extremely unusual, movements which were fundamentally normal occurred within the muscle groups. The skeletal structures showed marked modifications in responding to changes brought about by the growth of the transplant. In the skull the prechordal trabeculae were displaced and a new ring of cartilage was sometimes formed around the brain. The vertebrae of the trunk underwent a partial ankylosis. Since the nervous mechanism in the trunk region was normal, the excessive chondrification was not thought to be due directly to mesencephalic removal.

WYMAN, Boston.

REPORT OF A CASE OF BLINDNESS RESULTING FROM SEROUS MENINGITIS WITH RETURN OF NORMAL VISION FOLLOWING DECOMPRESSION. A. RIFAT and F. MOUHIDDIN, Ann. d'ocul. **166**:716 (Sept.) 1929.

The authors report a case of blindness resulting from serous meningitis. Decompression was followed by the return of normal vision. Bilateral papilledema was evidently the cause of the loss of vision in this case, and measured 5 diopters in the right eye, and 3 diopters in the left.

A CASE OF TEMPORARY BLINDNESS DUE TO ANGIOSPASM OF THE RETINAL ARTERIES IN A PATIENT SUFFERING FROM MALARIA. JEAN SÉDAN, Ann. d'ocul. **166**:705 (Sept.) 1929.

Spasm of the retinal arteries lasted for three days; antispasmodics were of no avail, and the entire retinal circulation seemed to have been arrested.

BERENS, New York.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 21, 1929

LOYAL DAVIS, M.D., *President, in the Chair*

THE SYMPTOM OF LHERMITTE IN MULTIPLE SCLEROSIS. DR. HUGH T. PATRICK.

In 1924, Lhermitte, Bollack and Nicholas called attention to a symptom of multiple sclerosis presumably not previously described. This was "pain" like an electric discharge brought on by flexion of the neck. They reported one case. The patient was a woman, aged 43, and there is no reason to doubt the diagnosis of multiple sclerosis. When she flexed the cervical spine, a sensation like that of an electric current started from the back of the neck and coursed along the spine and into the extremities. The intensity varied. When bad it reached to the fingers and toes. It was also caused by flexion of the trunk. Three years later, Lhermitte, Levy and Nicholas reported further on the symptom, adding two new cases. A month or two after this, cases were reported by Roger, Rebould-Lachaux and Aymes (four cases) and by Trioumphoff (two cases).

Finally, one of Lhermitte's patients came to New York, was shown at the New York Neurological Society by Wechsler and gave rise to some discussion with considerable difference of opinion. This led Lhermitte to write another brief paper on the subject which was published in the ARCHIVES in July, 1929.

In all his communications, Lhermitte has insisted on the comparison of this sensation to that of an electric shock or an electric current. Apparently he took over this comparison from his patients, without specifying what sort of shock or what sort of current. Obviously, what occurs is more or less acute tingling. One of Trioumphoff's patients positively rejected the electric comparison. Another patient never thought of the comparison, but when it was suggested said yes. One patient did compare it to a faradic current. The patient shown by Wechsler was an electrician (also obviously a neurotic); he compared his sensations to what he felt when, in repairing an electric lamp, he received some of the current. In one of his papers, Lhermitte likens it to the peculiar tingling caused by percussion of an injured nerve. No one seems to have thought of comparing it to such a homely thing as what one feels when he receives a bump on his "crazy bone," to my mind a handier comparison.

More than once, Lhermitte asserted that this symptom is confined to two diseases of the cord: multiple sclerosis and what he calls concussion of the cord. But, of course, "concussion" is not a "condition." In another place he calls it system degeneration of the cord from trauma (dégéneration cordonale traumatique), in other words, the condition following a bruise or more severe laceration of the cord.

In any event, this dictum is far too dogmatic. Tingling of the extremities brought on by flexion of the cervical spine is known to occur in tumor of the cord, cervical Pott's disease and probably in other lesions. This is the reason why I present this patient, who presumably has incipient multiple sclerosis and who at different times has presented the symptom of Lhermitte. I do not recall having observed the symptoms before in this disease, so when it first appeared in this patient I thought that possibly I had made a diagnostic error. Lhermitte insisted that it is an early symptom and consequently of considerable diagnostic value. In view of its rarity in multiple sclerosis and its occurrence in other diseases, I think that as a diagnostic aid it is not very significant. But it is well to know that it may occur in this disease. In my patient it did not occur very early.

A man, aged 28 at the time of presentation, was first examined in August, 1926. The anamnesis was unimportant. He said that he had not had venereal disease. He was intelligent, educated, somewhat emotional and a competent business executive. He had a high degree of myopia and some astigmatism. In March, 1926, he began to have a numb, cold, tingling feeling in the feet, and when barefooted he had a feeling as if something thick were between the feet and the floor. He thought that he was more careful than usual in using the feet and legs but was scarcely conscious of any disability. The sensation gradually ascended the legs as far as the upper part of the thighs and was worse when he was much on the feet. This gradually disappeared, having been present for only two or three weeks, and he remained well until two weeks before I saw him. At the end of a vacation of two weeks, during which he had driven a car 1,700 miles, 450 miles in the last two days, the numbness of the feet returned. After two days, it was felt more in the knees: a feeling of coldness, numbness and tingling. In the next five days it became worse and ascended so that when I saw him it had reached the waist line. Two days before, he had noticed numbness of the last three fingers of both hands. The "seat" also felt numb so that fecal evacuation did not feel normal.

Examination showed distinct, if slight, signs of organic disease. The pupils and eye movements were normal; there was no nystagmus. The deep reflexes were about normal, but the achilles jerk and knee reflex were slightly greater on the right side. Occasionally, the Babinski sign could be elicited on the right. The right cremaster reflex was slightly less than the left. The abdominal reflexes were brisk, but the left was distinctly greater than the right. It should be noted, however, that he had a large cicatrix on the right, the result of an operation for appendicitis. There was no anesthesia, except perhaps slight anesthesia of the glans penis. The left lower part of the back, from about the first lumbar region to the midbuttock, was slightly hypersensitive to touch, prick and thermal impressions. Vibration sense was greater at the left than at the right malleolus. The gait was slightly paretic-ataxic, but tests showed no distinct incoordination. There was no intention tremor. The Wassermann reaction of the blood was negative. He was put to bed for a month and small doses of iodide were administered. The unpleasant sensations nearly disappeared. He could walk well, but not perfectly; he could stand on either foot with the eyes open but not with the eyes closed. There was no Babinski sign. The achilles jerks were exaggerated, the right slightly more so. The cremaster reflexes were equal and normal; the abdominal reflexes were as before. There was slight anesthesia to the tuning fork on the ring and little fingers. The test tube test showed slight, rather rapid intention tremor, which was more noticeable on the left.

On Oct. 19, 1926, he was still better, though the symptoms had not disappeared. If, while seated, he inclined the head forward, a pain shot down the spine and legs to the feet; there was no pain in the arms. The spinal fluid, when examined on December 8, was clear, with a scarcely visible trace of globulin, five cells, Wassermann and Lange tests negative and no excess of albumin. The Queckenstedt test was negative. By Jan. 31, 1927, the symptom of Lhermitte had nearly disappeared. Occasionally, on flexing the neck he felt tingling in the right thigh. On March 28, the tingling in the thigh on flexing the neck had disappeared. Signs of organic disease were very slight on May 27. Numbness of the last three fingers continued; sometimes it was difficult for him to recognize coins in his pocket. After walking rapidly, when he sat down he felt tingling in the toes and over parts of the legs, but there was no more tingling on flexing the neck. He was able to run up and down stairs.

On September 9, he reported that during the summer he had walked as much as 4 or 5 miles, piecemeal, in half a day. He took some rhinitis tablets for a cold and could not micturate for eight or ten hours. Some days later, this experience was repeated, after which occasionally the stream was slow to start.

On Jan. 13, 1928, Lhermitte's sign could not be elicited; but by May 8 it was again in evidence, and numbness of the hands and about the trunk was very

annoying. He was put to bed for ten days and these symptoms disappeared, except for some numbness of the fingers, but after being about for a week Lhermitte's symptom returned. During the summer it disappeared.

On March 15, 1929, the results of an examination were much as before but there was no intention tremor. About the end of August, for a couple of days, and again for a like period in September, flexion of the neck caused a transient sensation of burning in the right knee. There was no symptom of Lhermitte at the time of presentation.

DISCUSSION

DR. D. M. OLKON: Do you consider that this symptom is due to an angiospasm?

DR. GEORGE W. HALL: How is the symptom of Lhermitte explained in this case? Does not Dr. Patrick think that more definite symptoms of multiple sclerosis should have developed by this time? Everything that has been described can be explained on a functional basis. The patient gave no history of early eye symptoms. The abdominal reflexes are present and about the only positive feature, it seems to me, is the occasional Babinski sign.

DR. HUGH T. PATRICK: I do not consider this an angiospasm. Lhermitte's explanation of this symptom, which he presents as tentative, is that it is due to the action of the plaques of multiple sclerosis on the nerve fibers. Starting from war cases in which a nerve, that was injured but not destroyed, would produce this sensation when percussed or stretched, he described this symptom in cases of injury to the spinal cord, which were also war cases. His reasoning is: That in these cases the axis cylinder is there but the myelin sheath is absent; the myelin sheath being a protection for the nerves, prevents this symptom from occurring in a normal cord. The pathology of multiple sclerosis corresponds to the conditions in which the axis cylinders remain undisturbed but the myelin sheaths disappear. Flexion of the neck in multiple sclerosis causes pressure or tension on the cervical cord, according to Lhermitte; hence, the symptom. I do not know about the tension, but this symptom occurs in tumors of the cervical cord and flexion of the neck would cause pressure on the cord and produce the tingling sensation.

I do not know that this is a case of multiple sclerosis but believe that it is. I think that the case cannot be explained on a functional basis. I have seen the patient regularly and there has practically always been something indicating organic changes. While he is at times emotionally upset he does not exaggerate the symptom of sensation. He had a nervous chill after driving his car on one occasion, and on one other occasion he fainted when he was vaccinated, but that is not an uncommon occurrence. He also fainted when he had a bad attack of shingles on the back. The Lhermitte symptom comes and goes. There have been times when he could not run up and down stairs, and on one occasion when I saw him his gait was distinctly of organic type. In my experience, when a case looks like a cord lesion and one cannot find anything satisfyingly definite it usually turns out to be multiple sclerosis.

FURTHER REMARKS CONCERNING MEDULLOBLASTOMAS: THE EFFECT OF ROENTGENOTHERAPY. DR. PERCIVAL BAILEY.

This article will be published in full in a later issue of the ARCHIVES.

NERVOUS AND MENTAL PHENOMENA ASSOCIATED WITH PAROXYSMAL TACHYCARDIA. DR. FREDERICK P. MOERSCH.

It is my purpose here to call attention to the various nervous and mental manifestations which may be associated with paroxysmal tachycardia. Neurologists or psychiatrists are prone to consider tachycardia as belonging to the domain of the internist, and as a consequence to overlook a syndrome which has frequently associated with it distinct nervous or mental phenomena. These phenomena may

be so marked and may present such a variable picture as to mask the underlying cause, giving rise to many misconceptions and leading to incorrect diagnosis.

Bouveret, in 1889, coined the term "tachycardia essentielle paroxystique." He published an exhaustive and masterly review of the subject and left comparatively little to add other than details, reports of unusual cases and the more recent and important electrocardiographic studies. Schlesinger was the first to make a thorough study of paroxysmal tachycardia in relation to the central nervous system. With the advent of the electrocardiograph, added light was thrown on paroxysmal tachycardia. In 1924, Willius and Barnes presented an exhaustive and careful study of the subject. In a supplementary study, Barnes called attention to the various cerebral manifestations associated with this disorder.

Paroxysmal tachycardia may be defined as a condition that is characterized by the following features: (1) sudden change in the normal cardiac mechanism, producing a rapid rate, varying between 120 and 250 beats a minute; (2) the patient may or may not be entirely conscious of the great degree of cardiac acceleration; (3) the attack generally covers a definite period of variable length, from minutes to hours, or even, rarely, days; (4) the tachycardia not only begins abruptly but usually ends abruptly, and (5) cerebral phenomena may be associated with the attack and may tend to dominate the clinical picture.

Paroxysmal tachycardia is slightly more prevalent in males than in females. The greater number of patients present themselves between the fourth and sixth decades of life. Exciting causes are endless and belong to the conditions usually associated with functional disorders. The attacks may, however, have no apparent exciting factor and may occur without warning and even during sleep.

The outstanding factor regarding the pathology of paroxysmal tachycardia is the absence of organic changes. The nervous and mental symptoms are probably secondary to interference with the normal cerebral circulation. Owing to the rapid beat of the heart the ventricles fail to fill properly and, as a result, the volume of the flow of blood to the brain is decreased, resulting in symptoms usually attributed to cerebral anemia.

The important point from the standpoint of the physician is to keep the condition in mind and in the presence of recurring, unexplained cardiac or cerebral phenomena, to question closely concerning the exact symptoms. If possible, an attack should be witnessed and an electrocardiographic tracing obtained.

The diagnosis of paroxysmal tachycardia is comparatively simple if the possibilities of the condition are kept in mind. Many of these cases are classified under the heading of cardiac neurosis, but it would seem certain that one is dealing with a distinct entity that merits special consideration.

The frequency of nervous and mental symptoms in paroxysmal tachycardia varies considerably. In about 20 per cent of cases of paroxysmal tachycardia seen at the Mayo Clinic, mental phenomena of varying degree were encountered. Definite nervous manifestations are somewhat less common. They occurred in the same group of patients in about 15 per cent of the cases. Among the more common nervous phenomena are varying degrees of vertigo, syncopal attacks, visual disturbances such as temporary blindness and scotoma, attacks of unconsciousness, transitory aphasia and paresthesias. Among the more common mental phenomena are anxiety, depressions and agitation, rarely mild delirium.

The prognosis in cases of paroxysmal tachycardia without signs of organic cardiac disease is good. The attacks are compatible with long life, but if the attacks occur in conjunction with organic cardiac disease the prognosis is determined by the type of the underlying cardiac injury. That the condition must not be treated lightly is evident from the fact that I have seen death occur as a result of a paroxysm in three patients.

Of paramount importance in the treatment for paroxysmal tachycardia is the recognition of any pathologic change in the heart. The elimination of toxic agents, such as alcohol and tobacco, is important, as not infrequently a reduction of smoking alone may lessen the frequency of the attacks. Vagal pressure may abort an attack. Quinidine sulphate given in doses of 3 or 4 grains (0.195 or 0.260 Gm.)

every three or four hours appears to be the most helpful remedy, as it tends to depress the irritability of the auricle.

Conclusions.—1. Paroxysmal tachycardia is of fairly common occurrence, and because of its associated nervous and mental manifestations merits the consideration of neurologists and psychiatrists.

2. Its chief characteristic is its abrupt onset and cessation.

3. It is more common in neuropathic persons, and there may be other evidence of functional disturbances.

4. The presence of organic pathologic changes in the heart need not influence the clinical picture although the prognosis varies with the degree of cardiac injury.

5. The nervous and mental phenomena may vary from slight anxiety or dizziness to delirium or convulsions.

6. Although it is not possible to establish either an isolated etiologic factor or a precise pathologic lesion, paroxysmal tachycardia represents a clinical entity and should be so recognized.

DISCUSSION

DR. D. M. OLKON: Vaquez, Lewis, McKenzie, Osler and others are of the opinion that in most instances of paroxysmal tachycardia one should keep in mind the possibility of its being caused by a disturbance of the intrinsic cardiac mechanism, in the bundle of His, the nodes, myocardium or in the vagus balance. That the myocardium may suffer fatigue and loss of tone is obvious, for normally, physiologists tell us that the heart pumps from 300 to 400 or more liters of blood per hour, and in tachycardia, when oft repeated, the increased contractions may increase the work of the heart muscle, thereby causing myocardial tonus disturbances. It is also reported that no changes have been found either in the myocardium or in the nodes in some of the cases of paroxysmal tachycardia. That is not saying, however, that no damage occurred in the conductive apparatus, or that recurring paroxysmal tachycardia is an innocent affair.

DR. ALFRED P. SOLOMON: I am interested in the acceleration of the heart rate in phobic persons. My attention was first called to this in a case which Dr. Favill and I studied together. The patient was a typical phobic, who presented a pronounced tachycardia and precordial symptoms during his panics. At the time, my attention was called to one of Dr. Favill's papers in which he described his ability voluntarily to accelerate his own heart. Since then I have studied phobic patients during their attacks of panic and have repeatedly observed that they show a marked acceleration of the heart rate; coincidently, they exhibit many of the mental symptoms which Dr. Moersch has described. I have never seen the rate over 150, except in one case when it was consistently around 230 during the attacks. This patient was referred to me by a cardiologist who found no evidence of paroxysmal tachycardia by electrocardiographic study.

It has been possible for me to produce tachycardia in phobic patients with the use of hypnosis by suggesting the inciting fear state. In all of these patients I have been surprised to note that there is a very definite beginning and an end to their attacks and that the degree of tachycardia is in proportion to and terminates with the mental symptoms. Sometimes the patients are alarmed by the cardiac symptoms and complain primarily of them. In my cases the state of mind is obviously the primary factor. I wonder if in cases of true paroxysmal tachycardia with mental symptoms the same condition does not exist.

DR. HUGH T. PATRICK: I think that this paper cannot be adequately discussed in a few minutes. In his presentation, Dr. Moersch seems to me to have sacrificed accuracy and definiteness to brevity. It contained too many vague expressions and statements. He said that some of the patients have organic heart disease and some have not, with no hint as to the significance of these facts. Some of the attacks are accompanied by "cerebral symptoms." Some patients have "syncope." To any one familiar with the various forms of syncope and pseudo-syncope this statement brings no illumination. The essayist spoke of "dizziness" and "vertigo"

with no apparent effort to discriminate. That many patients complain of dizziness who have no dizziness at all is notorious. Much less have they vertigo. He says that some attacks of paroxysmal tachycardia are accompanied by emotional disturbances, without indicating their relationship. He does not even state whether in his opinion paroxysmal tachycardia is a pathologic entity or just a symptom complex of various causation.

That emotional states may cause the pulse suddenly to go to 140 or more, so to continue for a longer or a briefer period, then quickly return to normal, I think, is fully established; this in persons with no evidence of organic cardiac disease. But is such tachycardia to be called "paroxysmal tachycardia" or not? The author does not tell us.

Dr. Frederick P. Moersch: As to the question of pathology, Dr. Yater studied a group of hearts carefully and could find no evidence of organic heart disease. This does not prove conclusively that there is no cardiac pathology but it is safe to say that as far as we have been able to determine, no specific cardiac lesion has been made out. McKenzie, in his book, by no means settles the question of pathology. Schlesinger, in his series of cases, found vagal masses, which he supposed to be factors in producing tachycardia. As time went on, cerebral tumors, syphilis, etc., were assumed to be causative agents. With the advent of the electrocardiograph, paroxysmal tachycardia has been placed on a definite basis and there is no longer any reason for assuming it to be a neurosis.

I brought this subject up because I think that it is a definite syndrome. I do not know the exact cause but I know that many cases of paroxysmal tachycardia are incorrectly diagnosed as epilepsy, cardiac neurosis, hysteria, etc., when as a matter of fact they present a definite entity and should be so recognized.

Manic-Depressive Pschyosis in Private Practice: Length of Attack and Interval. Dr. H. A. Paskind.

This article will be published in full in a later issue of the Archives.

The Action of Hemolytic Toxins on Nervous Tissue. Dr. Arthur Weil.

This article appeared in full in the April issue of the Archives (**23**:789, 1930).

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Thursday, Nov. 21, 1929

Donald J. MacPherson, M.D., *President, in the Chair*

A Case of Unilateral Choreomyoclonic Movements in a Young Epileptic Patient. Dr. Paul T. Yakovlev.

M. B., aged 18, came from a healthy stock, was born at full term, and grew and developed normally. At the age of 8, in 1919, he had pneumonia complicated with empyema. He was sick for four months; recovery was slow but complete. He went to school and had no difficulties in studies. When he was in the second year of high school, in February, 1927, he was taken ill rather suddenly with acute nephritis; he had high blood pressure, heart decompensation, lung congestion and fever. He was in a hospital for six weeks and recovered completely. He returned to school but could not follow his class. Four months later, in September, when swimming, he was seized with convulsions. One month later, at night, he had another fit in which he bit his tongue. Since these first two fits until the time of presentation, he had had four more major convulsive attacks, the last one being reported in February, 1929. Already, before the first attack occurred, he noticed that he sometimes had "jumps," as he called them, especially when

doing something; for example, when bending forward to pick up some object from the ground he would be thrown backward by sudden contraction of the back muscles. These "jumps" and "starts" also occurred in his arms and shoulders. They occurred usually before the convulsive spell. In December, 1928, he was admitted to the Monson State Hospital. On admission, examination of the heart, lungs and kidneys gave negative results. He had a normal blood pressure of 110 systolic and 78 diastolic. A lumbar puncture was performed in January, 1929, and gave negative results. A second lumbar puncture, in August, again gave negative results. Following this lumbar puncture and for three days the patient had a rather severe myoclonic attack, during which he had, almost continuously during the three days, "jumps" and "starts" in the head, shoulders, arms and legs, with contractions of the diaphragm, that disturbed the respiratory rhythm. The patient was in bed and complained of headache. At this time examination revealed distinct and coarse horizontal nystagmus, more pronounced when looking to the left. Three or four days later the myoclonus disappeared and nystagmus was no more noted.

Neurologic examination on the whole gave negative results, except that there was some swaying backward when standing in the so-called Romberg position with the eyes shut. In February, the patient returned home and stayed out of the hospital until the latter part of June, when he was readmitted. During this time he had only one convulsion; otherwise he was feeling well, though his mental condition showed considerable impairment. He was somewhat slow in thinking and was unable to give accurate information about his condition. About two weeks after he came back to the hospital, he began to have at first mild, later more severe, involuntary muscular contractions in the right arm and right leg, together with involuntary movements in the fingers of the right hand and in the toes and ankle of the right foot. He had not noticed this movement himself, but his attention was attracted to it by others. These movements, since their onset, had persisted without much variation, except that they tended to become rather more severe. They were limited to the right arm and right leg and were never observed on the opposite side of the body, in the face or in the trunk. They were unceasing during the whole day, disappearing only when the patient was asleep. They were distinctly more pronounced in the morning than in the later part of the day. Emotion and fatigue increased them. They did not seem to disturb, at least at the time of presentation, the voluntary movements, the patient being able to play tennis. He said, however, that he "loses grip" often in his right hand and sometimes his right leg "gives way." These involuntary movements consisted of myoclonic contractions, especially in the muscles of the shoulder and forearm and in the muscles of the thigh, and of involuntary movements somewhat like chorea in the fingers and toes on the right side. These last movements consisted of drumming movements of the fingers, "pill rolling" of the index finger and thumb, flexion-extension of the wrist, flexion-extension of the toes and rotation of the ankle. Extraction of a tooth necessitated the administration of ether anesthesia. When going through the first effects of the anesthesia there was distinct exaggeration of the involuntary movements in the right side, especially with regard to the myoclonic component. The movements completely disappeared under full anesthesia, reappearing again with the same intensity when coming out of the anesthetic. Scopolamine hydrobromide was given for therapeutic purposes, but the patient claimed that it made "twitching" and "shaking" in the right arm and right leg rather worse and refused to continue this medicine.

Neurologic examination during the last few months showed the following: There was distinct hypotonia of the right arm and right leg with diminished reaction of antagonists and increased passivity in the right arm and the right leg. Moreover, muscular force seemed to be diminished in the right hand as compared with the left. There is also some ataxic element when performing diadokokinesis tests and past-pointing tests, without showing actual adiadokokinesis or definitely oriented past-pointing. Tendon reflexes were present. The left styloradial and left patellar were more active than their mates on the right side. The abdominal reflexes were weaker on the left side. There was some diminished sensibility

on the right side of the body. Vibration sense was perceived sharper on the left side than on the right. A cold tube was always "cooler" on the left side than on the right. A pin prick "pricked" more on the left side than on the right. Touch sensation did not show a difference on the two sides and did not show any deficiency. In the face, a cold tube and pin prick were equally perceived on the two sides. The vibration of a tuning fork seemed to be heavier, "more buzzing," on the left than on the right. A Bárány test was negative, the patient showing normal reactions after irrigation of each ear with cold water. The eyegrounds were normal. When standing in the Romberg position, there was always some swaying backward and toward the right side. Plantar flexor reflexes were present on both sides. There was no Oppenheim sign and no clonus of the foot. Scopolamine hydrobromide was injected hypodermically in a dose of $\frac{1}{100}$ grain (0.00065 Gm.). During the first fifteen minutes after injection, there was a noticeable increase of the myoclonic component of the involuntary movements of the right arm and leg. At the same time, tendon reflexes on the left side became distinctly exaggerated and a tendency to an extensor response of both sides was noted. Within half an hour after the injection, the patient became extremely sleepy, so that he could hardly be aroused for examination. Choreomyoclonic movements appeared to be somewhat diminished in range and intensity. Distinct bilateral pyramidal symptoms developed with a positive Babinski sign, Oppenheim sign, and a suggestion of clonus on the right side, and distinctly exaggerated tendinous reflexes on the left side. Within about forty-five minutes, involuntary movements completely disappeared; the patient was sleeping. Pyramidal symptoms persisted on both sides. The same observations were made two and three hours after the administration of the scopolamine. The patient fell asleep and slept until the next morning. The next morning the movements seemed to be even more pronounced than usual. He had distinct myoclonic contractions in the trunk, shoulders, arms and legs, with frequent diaphragmatic contractions disturbing respiratory rhythm.

I believe that it is of interest to present this case on account of the rather definite previous history and the onset of the involuntary movements while the patient was under observation, as well as because of the character of these movements both myoclonic and choreic in type and strictly localized to the right side of the body. I would not venture the localization of the organic lesion causing this particular hyperkinetic syndrome; however, cerebellar feaures in the right side of the body with mild pyramidal features on the left would suggest a midbrain localization.

DISCUSSION

DR. E. W. TAYLOR: Is there any possibility in this case of an antecedent encephalitis?

DR. YAKOVLEV: It is very possible. Nephritis is one of the manifestations of encephalitis, not necessarily epidemic. Apparently it is not a tumor, of which one might think at first glance.

"EARLY PSYCHIC INVALIDISM" IN RUSSIA. DR. J. KASANIN.

A new clinical syndrome has been described in the Russian psychiatric literature by Gannushkin and his students in connection with the experiences in the World War, the Revolution and the Civil War, under the title of early psychic invalidism.

The syndrome consists in early intellectual impairment occurring in people in their twenties and early thirties who have been under constant strain of the aforementioned conditions. In addition to the intellectual involvement there is a marked let up in the energy output, irritability, tinnitus, emotional outbursts and definite reduction in the total efficiency of the patient in his usual occupation. The clinical picture resembles early cerebral arteriosclerosis. The patients who were shown to me have, until recently, occupied important executive positions.

Steffko went over the pathologic material and classified it according to the previous occupation of the patients. People who were unprepared for intellectual work, but who were suddenly thrown into a position of high responsibility, showed a marked arteriosclerosis of the brain as compared with the ordinary manual workers or people who were especially trained for intellectual work. The conclusion reached is that prolonged and unusual emotional and intellectual strain results in early appearance of arteriosclerosis in the brain.

THE SIGNIFICANCE OF LOCAL FACTORS IN CIRCUMSCRIBED (ELECTIVE) PATHOLOGIC PROCESSES IN THE BRAIN. DR. WALTER SPIELMEYER.

This paper will be published in full in a later issue of the ARCHIVES.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Dec. 3, 1929

LOUIS CASAMAJOR, M.D., *President, in the Chair*

THE INFLUENCE OF FUNCTIONAL CIRCULATORY DISTURBANCES OF THE CENTRAL NERVOUS SYSTEM. WALTHER SPIELMEYER, München, Germany (by invitation).

Anatomic investigation shows that the variety and spread of changes can be of circulatory origin without change in the size of the lumen of the vessel or pathologic changes in the vessel wall. It can also be proved anatomically that a nonorganic obstruction to the circulation may cause a degeneration of the central nervous system; in other words, a disturbance of the circulatory function only may produce conditions similar to those which are caused by an organic occlusion of circulation. The foci will appear the same, and yet one resulted from a distinctly recognizable occlusion of the vessel and the other developed without such an obstruction. In cases of arteriosclerosis with hypertension, I have long observed that foci of alterations are found not only within the reach of vessels narrowed by the arteriosclerotic process, but also in parts of the brain which are provided for by intact arteries.

It is not necessary today to bring new proof for these similarities in the effect of organic and of functional alterations in the circulation. Today and here, it is more important for me to show how, from the most opposite causes, damage strikingly similar can result in the brain.

One finds the same alteration in traumatic lesion, carbon monoxide intoxication, morphine intoxication, chloroform narcosis, hypertension, pseudo-uremia, and after other spasmodic conditions. One sees always the same alterations. They differ only according to their age and intensity. When they sometimes seemed to be different in their localization and something really typical seemed to be in them, further experience showed that that was an error. So these observations mean nothing for the definition and classification of disease entities. Their fundamental value consists rather in showing something common to all those diseases, etiologically and clinically so very different; not anatomic forms of disease but pathogenetically similar complexes of symptoms. The essential result of these observations is the predomination of central circulatory alterations in brain injuries caused by the most different noxa, such as trauma, intoxications, infections, hypertension or eclampsia. It can be seen from this how the most varied injuries by a more or less long chain of causes finally lead to the same pathophysiologic process.

From this, one may conclude what meaning these determinations have in neurologic and psychiatric questions. I think they give an understanding of the essence of these brain alterations. And besides, pathogenetic analysis leads, through

knowledge of the development of brain conditions, into pathophysiology. And through pathophysiology, which is evident morphologically, one understands many clinical symptoms.

One tries to make use of the microscopic observations in the interpretation of clinical symptomatology. After all, as I have said before, this can be done only in cooperation with the clinician. He reports when focal symptoms of the aforementioned kind are present — apoplexies, paresis, convulsions in youthful hypertonic patients, eclampsias, eclamptic intoxications and traumatic conditions. The photographs demonstrate the anatomic background of such circumscribed cerebral manifestations. Consideration of the fresh necrobioses which appear only as a faint pallor, has been neglected for a long period of time, but many so-called hemiplegias without anatomic changes can be explained by these pallors, visible only in Nissl preparations. It is the same with general symptoms of cerebral origin: sudden drowsiness and coma, excitement with anxiety and signs of acute delirium. Such general cerebral symptoms can occur in relationship with widespread vasomotor disturbances, which acted on large parts of the brain tissue. In most cases a special vessel district, as, for instance, the district of the arteria cerebri media, or posterior, was especially involved on one side. Sometimes the same district on the opposite side also showed some damage, and in a few cases there were alterations in very different vessel districts.

One also knows psychic symptoms — for instance, in intoxications — which according to my experience I connected with circulatory damage, but which showed no visible morphologic substrate. One must suppose that here the central circulatory disturbances were not yet strong enough to destroy the nerve tissue. To produce visible alterations in the tissue a certain intensity of circulatory deficiency is needed. Such cases explain the possibility of total recovery and of the disappearance of menacing symptoms.

In morphine intoxication, for instance, these observations are very impressive. From the appearance and disappearance of symptoms, as well as from the frequently observed increase and decrease of their intensity one can conclude that the angiospasms or stases vary in degree. This may explain hemiplegia, its varying intensity and its final disappearance, as well as the different degrees of unconsciousness, the increase into coma and the final recovery. The angiospasm and angioparalysis may be followed by recovery of the vasomotor functions.

Certainly, these statements still need control and confirmation. Nevertheless, they mean that some progress has been made by demonstrating that brain alterations and symptoms are not, as formerly believed, directly caused by the toxic or traumatic influences, but mainly by their effect through circulatory changes.

There is, in general, no other topic in psychiatry and neurology for which the anatomist is so much in need of the help of the clinician in order to analyze not only medical, but also purely anatomic questions of natural science.

DISCUSSION

DR. BERNARD SACHS: I appreciate the excellent way in which Professor Spielmeyer presented the subject; he has opened up a number of interesting questions which have been agitating many of us for a number of years. As he began his presentation I thought that he would present definite evidence on a subject which was discussed in America thirty years ago; namely, whether or not there was such a thing as spasm of the cerebral blood vessels; a great many lesions which were supposed to be functional were explained as mere spasm of the blood vessels. Whether Dr. Spielmeyer believes that there is such a thing or not would be of interest. I think that his explanation is most plausible, but I was also impressed with the fact that what he speaks of as a functional condition is a more or a less complete occlusion of a vessel — whether the vessel is actually occluded by a thrombus or whether it is practically occluded by a narrowing of its walls, as would be the case in marked arteriosclerotic changes of the walls. I would like to ask Dr. Spielmeyer (he may not know that we have a great way of asking questions in our discussions), whether it would not

be wise to bear in mind the possibility that some lesions may after all be the result of venous stasis rather than of arterial occlusion, partial or complete; it occurred to me particularly that that might be the case, because one knows that in chloroform narcosis, and especially in whooping cough, a number of cerebral symptoms and cerebral conditions arise from a considerable amount of venous stasis. Dr. Spielmeyer mentioned a case of whooping cough that lasted only a few days; it is a question whether, in this case, venous stasis might not be responsible for such changes as are presented in these various slides.

DR. E. D. FRIEDMAN: May I add a word of confirmation from the clinical side, to the graphic demonstration by Prof. Spielmeyer? For the last three years we have made use of encephalography in the study of various cerebral conditions, such as degenerative disease of the brain, hypertensive syndromes, epilepsy and postconcussion states. In all of these cases we have found striking deviations from the normal encephalogram. They consist of enlargement of either one or both ventricles, increase in the surface markings and, at times, dislocation of the ventricular system toward the side of the lesion. It is my impression, too, that the encephalograms are not characteristic of any single condition — one obtains similar pictures in degenerative disease of the brain, in epilepsy and in the postconcussion state. Evidently there must be a common mechanism underlying all of them. This is most likely a vasomotor disturbance in the vessels of the brain. Professor Spielmeyer has demonstrated evidence in support of this hypothesis. The areas of necrobiosis which he has shown are apparently the result of vasomotor disturbances with resulting ischemia.

That the cerebral blood vessels have a vasomotor innervation had been long suspected by Pal and others who described angiospastic cerebral syndromes. It remained for Forbes, Wolf and their co-workers to provide the experimental proof for this hypothesis. Professor Spielmeyer has now demonstrated the pathologic basis for this important group of clinical entities.

DR. FOSTER KENNEDY: Dr. Hartwell and I, when operating on a conscious patient under local anesthesia, observed the exposed brain during an epileptic fit; the first episode of that epileptic fit was a chalk-white devascularization of the cortex. Before we could realize that the patient was going into epilepsy, we saw the cortex blanch as white as chalk. This was followed after four seconds, by a tremendous engorgement of the cortex, but there was no question that the cortex was first devascularized by a mechanism similar to that operating elsewhere in the body. It was a perfect visual demonstration of vasomotor control in cerebral tissue, and so a confirmation of Professor Spielmeyer's observations.

DR. SAMUEL BROCK: Do pathologic studies of viscera other than the brain bear out the vascular theory of Professor Spielmeyer in respect to these areas of degenerations? Is a toxic element, acting directly on the brain parenchyma, surely ruled out in Professor Spielmeyer's mind? Have any animal experiments been made in which purely vascular lesions, as produced by spasm-producing drugs, have conditioned necrobiotic changes comparable to those noted in his demonstrated cases?

DR. IRVING J. SANDS: What relation, if any, has cerebral edema to these degenerative changes?

DR. J. H. GLOBUS: It is because of modesty that Professor Spielmeyer did not stress the significance of the preparations which showed that areas of softening, occurring as the result of some functional disturbance in the circulation, are identical with those produced by an obstruction to the circulation. This is extremely important and is the experience of almost every neuropathologist, who often finds areas of softening without the ability to account for such alteration by changes in the vessels in proximity to that area. The question always arises, what is it due to? it may be explained by a vasospasm; it is also possible that some toxin had reached that part of the brain and produced the necrobiotic area, but the distribution of the areas is not in accord with the latter conception.

A selective area of softening can be accounted for only by a selective interference with the blood supply to that area. The material of Professor Spielmeyer throws a good deal of light on another condition, massive cerebral hemorrhage occurring in the young with no discernible lesion in a blood vessel supplying that area. Here again one needs an explanation. If one assumes that an area of softening has occurred at some time in the life of the patient, thus constituting a preexisting factor, and that at some later date there is a pronounced circulatory disturbance, then perhaps one finds an explanation for the fairly frequent occurrence of cerebral hemorrhage in young nonhypertensive persons without any recognizable change in the blood vessels.

DR. SAMUEL T. ORTON: One point which Professor Spielmeyer has not emphasized has interested me for many years; that is the differential action of partial starvation on the various elements of the central nervous system. In cases of arteriosclerosis one sees vessels that are only partially occluded, so that there is not a true softening with complete tissue loss but merely a neurocyte destruction. With a still greater reduction in blood supply one finds the neuroglia gone also; but even in such an area one finds the mesodermal cells still intact, as though they were able to maintain their integrity at a lower nutritional level than glia. One must thus consider several stages of tissue starvation: the first resulting in simple loss of function without tissue loss; then selective loss of the neurocytes, and finally neuroglia death resulting in cavitation.

DR. ARMANDO FERRARO: As Dr. Sachs has mentioned, for many years we have been faced with this problem, always debating as to the existence of true organic changes related to functional vasospasm. Since the World War, detailed studies have appeared dealing with this subject, among which I might recall those of Spielmeyer and of the French school led by Charles Foix. The latter author has studied extensively a case of hemiplegia in which, at the autopsy, he was unable to find any organic condition affecting the vascular system. Since then I have been interested in the subject, and I have been surprised to find frequently fresh areas of necrobiosis in various organic conditions. I was surprised to find that in some instances the blood vessels were intact and that no organic vascular condition could be called in as a cause of the necrobiotic process. In general arteriosclerosis, in paresis and in carbon monoxide poisoning I have had the same experience; although in the last condition I thought that necrobiosis might be the result of an acute swelling of the small blood vessels of the cortex. In epilepsy the same conditions are noticeable and I will mention it only to the extent of studies that Spielmeyer and his pupils have done of one particular region, i. e., the Ammon's horn, where most severe changes related to defective circulation are liable to occur.

It may be possible also that, in some so-called functional conditions accompanied clinically by increased psychomotor activity and vasomotor disturbances, one of the underlying causes may be an insufficient temporary vascularization of the cortex or of the vegetative centers.

DR. LOUIS CASAMAJOR: The lantern slides presented by Professor Spielmeyer are so clear that there can be no doubt that what he has shown is something real from the pathologic point of view. I was interested in his use of the word "functional"; for, to my mind, he used it correctly. In this country, at least, we are too prone to use "functional" as though it were synonymous with "psychogenic," which of course it is not. Professor Spielmeyer used it in the real meaning of the word. What he has shown tonight is a true functional disturbance of the cerebral circulation resulting in definite lesions in the brain.

PROFESSOR SPIELMEYER: I am sorry I cannot answer all the questions as I should wish to do. Some need not be answered because their authors agree with me, for instance, Dr. Casamajor and Dr. Ferraro, and I much appreciate the agreement of my colleague, Dr. Globus. There is no difference between my opinion and that of Dr. Orton concerning the different need of nutrition by various parts of the body. Of course, what one calls the functional parenchyma, the nerve

substance, is very much affected in comparison with the mesodermal connective tissue and the glia. Sometimes all the tissue can become necrotic, and sometimes only partial degenerations or partial necrobioses occur in such parts as are especially sensitive; it is true also that some areas are much more vulnerable than others. Not only is there the difference between the nerve substance and the connective tissue, but there are great differences between the nerve fibers and the nerve cells. In cases of partial necrobiosis one may have the nerve cells involved and the white matter below or above attacked in the least degree, so that one has here differences in vulnerability; it is not a special system that is attacked. That is not right.

Another question I cannot say much about is the connection between edema and these vasomotor disturbances. Some author has investigated this question. Jacobi and Magnus discussed it, but I never saw anything about the matter.

In regard to the question whether I have made experiments, I have done so; I have tried to observe the vessel function as Stanley Cobb did, but I do not wish to speak about this matter because I have no definite opinion on it.

I am very happy that Dr. Sachs agrees with the major part of my paper; I know that several decades ago there was considerable talk about vasomotor disturbance, especially by clinicians and French authors. At this moment I cannot remember what term the French authors used. Pal, in Austria, has the same idea and we are following his ideas, clinical and physiologic, and those of Volhard, in Germany, on kidney disease. But it was necessary to find the anatomic basis for these clinical observations and theories, and I think that I have.

I use the word, functional, in the same sense that you use it. In this connection the relationship between early, beginning, purely functional vasomotor obstruction and a true organic, material impediment to the blood flow. Both of these instances are observed in cases of arteriosclerosis with hypertension and are described in textbooks; but in some instances, with some blood vessels, one can explain by some organic impediment, and there are others in which one finds no sign of organic vessel disease. I agree with Dr. Sachs that one often finds stasis. I do not want to discuss this at length, but there is Ricker in Germany who was one of our first pioneers in this study from the anatomic point of view and who denies that any other functional disturbance of the circulation — as stasis or a prestasis — is the cause. I do not see that. I think there is a possibility that vasospasm also can produce partial necrobiosis. One knows better than to deny the so-called dead fingers, in neurotics, which may persist for hours without change in the stasis. This anemia can disappear, but if such a lesion occurs in the brain, why should this tissue not become necrobiotic?

I am glad that Dr. Kennedy spoke about his observation. In my little studies of the physiologic mechanism of the epileptic fit I have referred to these important observations of Kennedy and Dandy, which agree with those I have made.

SOME NEW METHODS OF STUDYING THE BRAINS OF EXCEPTIONAL PERSONS (ENCEPHALOMETRY AND BRAIN CASTS). PROF. C. VON ECONOMO, Vienna, Austria (by invitation).

Aside from the progress made in finding the physical basis of cerebral functions, it should be the aim and effort of modern neurohistology to look for the morphologic foundations of individual characteristics of man. Whatever these traits and capacities may be, their expression is effected through the medium of certain brain apparatus, and the study of the brain with this view in mind would be the anatomic approach to such characteristics. When any capacity of expression is so highly developed in a human as to elevate that person from the mass, one may assume that the brain of such a man might, if properly analyzed, help to shed light on the characteristic in question. Hitherto, however, the study of the brains of exceptional persons, whether talented musicians, great mathematicians or notorious criminals, has consisted merely in the weighing of brains and their preservation in alcohol or formaldehyde in some museum; or, at best, the sections made were stained for fiber tracts.

Modern cyto-architectonics and myelo-architectonics have shown that the cortex is a complex structure consisting of very many distinct areas. (Dr. von Economo demonstrated a special, new model of the brain, of his own design, which could be taken apart to show the gross delimitations in color.) That such fields might present individual differences is illustrated by a study of the area striata at the tip of the occipital lobe which, in certain races and certain of the apes, is developed to a much greater degree than usual and forms the so-called operculum occipitale. What relation such an over-development may have with the sense of sight, is not as yet known. Analogously, musical talent might be expressed in a special development of the first Heschl convolution.

In order properly to study the morphology of such areas or fields, it is necessary to exploit the most exact methods of modern cyto-architectonics. Dr. von Economo outlined his method of making cortical sections for such studies; it differs essentially from all former methods in that the sections are everywhere cut perpendicular to the convolution examined. The brain is thus sliced into a multitude of small sections. Since, probably, such destruction is what has kept us from examining the brains of exceptional persons, some other means than simple photography must be devised for preserving the totality of the brain, the outline of the skull, etc., before the brain is cut up. The important point is to achieve methods which deserve to become standard, for only in this way can such studies be of any general value. The details of the method are given in a paper in the *Zeitschrift für die gesamte Neurologie und Psychiatrie,* November, 1929.

The first step is to make a suitable cast of the brain and the skull. All former methods for making such casts have had serious disadvantages, mainly because they injured the cortex as a consequence of the inelasticity of the material used for the cast. By means of a happy invention of Dr. Poller, of Vienna, satisfactory casts can now be made. The substance used is a patented, elastic, mucilaginous mixture known as "negocoll." In the rigid state it is like soft rubber. It melts easily when mixed with some water and boiled, and can be smeared and poured over the brain. When threads are first laid over the surface of the brain, the cooled and hardened mass can be cut into several sections and afterward reassembled. The negocoll can be kept rigid by brushing with a second substance known as celerit, a waxlike material. Before the negocoll is removed from the surface of the brain, the median surface of the latter is also covered. When this median surface is lifted off, the brain can be taken out of the negocoll skull; the negocoll covering of the median surface can then be replaced, a hole cut, and a third substance known as hominit, can be poured in to make a positive cast of the brain. The hominit is a wax which melts and hardens easily, forming a permanent and true model of the brain. Such a model can be copied and recopied many times, for it is accurate in detail. To ensure that the true volume has not been made inaccurate by the spreading of the sulci of the brain after its removal, a cast of the skull can be made with hominit. The cast of the skull is strengthened by the addition of reenforcing wires to the material, as outlined in detail in the paper mentioned. The author demonstrated the materials used in casting as well as specimen casts of the brain and skull. It was shown how accurate measurements between fixed points could be executed on such casts.

Another important step, before sectioning the brains, is the accurate measurement of convolutions and surfaces. For this purpose the author constructed a net made of metal rods 1.5 cm. long, joined by carefully fashioned rings. The rods are divided by marks into sections of 5 mm. each. The brains are photographed twice in each of the six usual planes, first without the net, and then while covered with the metal net. This not only enables one to measure the length and breadth of convolutions or the distance between points, but also makes it possible to determine distances between fixed points. Since convolutions and sulci themselves may vary in size, the author has depended on the greater fixity of cyto-architectonic areal limits, and on this basis has listed twenty-six measurements between fixed points. He illustrated the method photographically, and discussed the details of measuring on the basis of microscopic studies of areas.

DISCUSSION

DR. BERNARD SACHS: I want to express the pleasure I have had at Professor von Economo's ingenuity in technic. His studies will probably lead to the revival, or perhaps the furtherance of a plan that has existed in America for a number of years, of which Professor von Economo may not know. A number of years ago, after the late Dr. Burt G. Wilder showed intense interest in the measurements of the surface of the brain, a society was formed to which the élite brains were supposed to be consigned. That society is still in existence, and I have no doubt your methods will be of help to determine whether or not talent has its special localization in different parts of the brain. Personally, and on behalf of the society, I want to thank you for what you have shown here.

DR. SMITH ELY JELLIFFE: I would like to add my word of sincere appreciation to that of Dr. Sachs. As I looked over the pictures shown here and also thought about the marvellous Atlas which Professor von Economo and Dr. Koskinas have prepared, my mind went back to the days of Gall and Spurzheim when genius was studied, first through the structures of the outside, i. e., through phrenology, not altogether to be derided, even at the present time; then, to the days of Broca and the beginnings of true localization of functional areas in the brain, which registered a great advance. Then came a period when it was impossible to say anything really intelligent about cerebral topography without serial sections which Dejerine insisted should be made. Then came before my mind's eye the work of the Vogts, of Brodmann and of von Monakow; now we come finally to the élite method of von Economo, a complete method that should be the standard for some time. It seems to me that we are very fortunate this evening in seeing this final stage in a series of processes of the study of cerebral topography and the localization of function which has been slowly evolving for the last 100 years.

Book Reviews

CONDITIONED REFLEXES: AN INVESTIGATION OF THE PHYSIOLOGICAL ACTIVITY OF THE CEREBRAL CORTEX. By I. P. PAVLOV, Translated by G. V. ANREP, Oxford. Price $9. Pp. 411, New York, 1927.

This volume by the man whose name has for years been identified with work on conditioned reflexes is especially welcome as it is a natural sequel to his first attempt at a general exposition of the subject. I am referring to the volume entitled "Twenty Years Experience of Objective Study of the Highest Nervous Activity of Animals" (reviewed in the ARCH. NEUROL. & PSYCHIAT. **17**:135 [Jan.] 1927). In that volume, which unfortunately has not been translated into English yet, the author gave an intimate view of the development of his work. The present volume which consists of a series of lectures given before the Military Medical Academy in Leningrad in the spring of 1924 represents the mature consideration of all the data obtained by the author himself as well as his co-workers up to that time. This volume, as the first one, is remarkable for the absence of any attempt at all inclusive theories and interpretations. It is merely a presentation of the results of years of investigations, results that after repeated tests have remained unaltered, and are presented in the form of objective observations. The interpretations which do appear interspersed through the different lectures, and to some extent concentrated in lecture 22, deal more with explanations of detailed investigations than with attempts at the formation of generalized theories. It would be well for one to read the review in the ARCHIVES of the volume mentioned. In that review an attempt was made to evaluate critically the relationship that exists between Pavlov's work and his method of approach and those of other investigators of animal (as well as human) behavior. Here I shall abstract some of the outstanding features of the actual results obtained.

Pavlov approached the physiology of the central nervous system with the aim of attempting a purely objective study of the functions on the same principle as would a physiologist in the study of any other organ of the human body. He was brought into this work through the medium of his studies of the digestive glands, especially the salivary secretions. In his attempt at a physiologic investigation of the control of the function of these glands by the central nervous system, however, he was confronted with two apparently distinct types, neither of which lent themselves to interpretation on the basis of one mechanism: 1. The introduction of certain substances into the mouth of the animal caused a secretion of saliva which was evidently of a type best suited for dealing with that particular substance. Thus, the introduction of dry, hard food caused a secretion of saliva that was rich in mucin and copious in quantity; the introduction of moist, soft food brought forth a secretion of a different type of saliva; the introduction of sand caused a secretion of watery saliva that was poor in mucin, etc. These phenomena could be approached on the basis of physiochemical reaction. Apparently, the contact of the food with the mucous membrane of the mouth stimulated the nerve endings in a certain fashion, and through a reflex arc the secretory reaction took place. 2. Nevertheless, the mere sight of food, in fact of a certain type of food, would cause an appropriate secretion of saliva. Furthermore, the sight of the man who usually fed the dog or even the sound of his footsteps as he approached the kennel would produce a secretion of saliva of a type that was appropriate to the food that the dog usually received. Here it would seem that there was no actual contact with the end-organs in the mouth and zoopsychologists and even physiologists who preceded Pavlov spoke of this type of reaction as psychic. In describing more complicated reactions of the dog, such as devotion to its master, expressions of hatred to others, etc., they spoke of such things as memory, feelings, intuition and what not, as being at the basis of the reactions of the animal. Pavlov took the view that no matter what sub-

jective experiences the dog might have during his reactions, one had absolutely no way of evaluating them scientifically. That all reactions of the dog observed in its behavior should be approachable on a scientific objective level, or else one must admit that none of the reactions can be studied physiologically, not even the so-called reflex reactions.

The first attempt at studying these so-called psychic stimuli demonstrated two important facts: 1. The stimuli in themselves did not necessarily have to bear any important relationship to the food. In other words, they could be indifferent stimuli as far as the food was concerned. 2. Whether they were indifferent or not they had to coincide on several occasions with the actual administration of food before the dog would respond to them alone as it did to the food that was administered. In other words, stimuli that in themselves had nothing to do with food could be conditioned to call forth a reaction similar to that which would be brought forth by the actual administration of food, after the two were made to coincide on several occasions previously. Thus, several repetitions of the ringing of a bell shortly before the administration of a certain article of food and continued for some time during administration could cause it to become an adequate stimulus for a flow of saliva which was appropriate for the type of food that was used. This mechanism Pavlov considered as being essentially of the nature of a reflex and he called it a conditioned reflex in contradistinction to a *nonconditioned reflex*, by which he understood the primitive reaction of the dog to the food introduced into its mouth. Another factor connected with this type of reflex soon became manifest. If, after a certain type of conditioned reflex to an indifferent stimulus was established, the indifferent stimulus was repeated on several consecutive occasions with only short intervals of two minutes each without the simultaneous administration of food, the secretion of saliva in reaction to the stimulus would gradually cease, and finally this conditioned reflex would be extinguished. The conditioned reflex, therefore, in contradistinction to the nonconditioned one was fairly easily developed, and just as easily extinguished. It had the disadvantage of instability but the important advantage of flexibility as compared with the nonconditioned one.

The ability to form and extinguish conditioned reflexes is advantageous. The animal at any given moment is subject to a constant flow of change in its environment. It brings with it into this constantly changing milieu a certain number of inborn, rigidly laid down, nonconditioned forms of reaction. They form the foundation of all its behavior, but actually comprise a small sector of the rich system of reactions which it presents to the observer. The greatest part of its behavior consists of new associations, i. e., of acquired temporary conditioned reflexes. The continuous changeability of the environment of the animal makes the provision for a similar arrangement in the animal not only valuable but necessary. The temporariness of the conditioned reflex gives the animal the means whereby it can adapt itself to changes in its environment. The formation of conditioned reflexes helps it to adapt itself to new conditions. The ready extinction helps in casting off the bonds that would hold it fettered to its old environment.

The first of these two types of reaction, that is, the conditioned reflex proper, is termed positive to distinguish it from the negative reactions of which extinction is one form. All the negative reaction forms are grouped by Pavlov under the term "inhibition," of which there are two general types: external and internal.

By external inhibition is meant the interference with or cessation of the flow of saliva in reaction to a conditioned stimulus when a totally new stimulus is brought in. Thus, if the sound of a bell was conditioned to cause a flow of saliva, the simultaneous flashing of a light would interfere with the reaction.

There are four types of internal inhibition: (*a*) Extinction (this has already been described). (*b*) Delayed reflex. Conditioned reflexes are formed by having the nonconditioned stimulus follow the conditioned one almost at once (in from three to five seconds). If after establishing such a reflex one repeats the process several times but allows an interval of three minutes to elapse between the con-

ditioned and the nonconditioned stimuli and then tries the conditioned stimulus alone, one will find a delay of from one and one-half to two minutes between the beginning of the conditioned stimulus and the flow of saliva. (*c*) Conditioned inhibition. The continuous repetition of the conditioned stimulus accompanied simultaneously by an indifferent one and not followed by the nonconditioned one will render the indifferent stimulus an inhibitory agent, if one repeats the same conditioned stimulus by itself, reinforced by the nonconditioned one. Thus, let the sound of a bell be conditioned to cause a flow of saliva. If now one repeats the sound of the bell with the effect of a flashlight for several consecutive times without the administration of food, and alternates this with the sound of a bell alone reinforced by the administration of food, the flashlight will become a conditioned inhibitor. (*d*) Differential inhibition. This is the mechanism which occurs in the differentiation of stimuli by the analyzers and will be taken up later. (*e*) Inhibition can also be produced by the continuous repetition of conditioned stimuli even if they are reinforced by the nonconditioned stimulus. As Pavlov describes it: "the isolated action of the conditioned stimulus, even though followed by the nonconditioned, leads to the development of a state of inhibition in the cortical elements and this development is quicker the greater the length of isolated action of each single conditioned stimulus and the more often such a stimulus is used." It is from this point that Pavlov approaches the mechanism of sleep and hypnosis. He regards the latest mentioned form of inhibition as partial, localized sleep. The combination of numerous stimuli to which the animal is subjected during the day gradually induces general inhibition of the cerebral cortex, which takes the form of sleep.

With the consideration of these fundamental principles as a basis, Pavlov proceeds to a discussion of the more complicated phenomena met with in his study of animal behavior. A clear understanding of these and their relationship to one another can be obtained only by a study of the original. Here will be given only a description of two of the most important phenomena:

(1) Differentiation.—Successful orientation of an animal in the constant flux of stimuli in its environment depends on a proper analysis of the latter. If a stimulus of a certain type is to serve as a signal of approaching food, by virtue of the fact that on several occasions it has coincided with ingestion of this food, then it is important not to confound it with other stimuli that are more or less similar to it. This process of differentiation has been shown to exist by actual experiments in Pavlov's laboratory. A conditioned reflex to a tone of about 1,000 vibration frequency has been established. At first this "signal" was confounded with tones of other frequencies within certain limits. By repeating the tone of 1,000 vibrations on several occasions, reinforced by food at the same time, and alternating this procedure by tones of other frequencies above and below 1,000 not reinforced, it was possible to get the animal to differentiate, e. g., between 1,000 and 1,012.

(2) A closely related phenomenon is that of irradiation and concentration. The mechanism of these two processes can best be illustrated by the following example: Five distinct points are taken on the skin of the dog's leg at equal distances from one another, the first at the shoulder and the last at the toes. The four upper ones are conditioned; that is, a certain tactile stimulation of these is followed by a certain type of food. A similar stimulation of the fifth point is repeated without food. Now, when one stimulates each of these points at long enough intervals, one gets a flow of saliva in the case of the upper four, and none in the fifth. The fifth point is now stimulated without effect on the salivary gland. After a short interval, the one nearest to it is stimulated, and there is no flow of saliva, whereas with an interval of shorter duration the excitation of the one second nearest gives a diminished flow of saliva; in the third the diminution is less, and the fourth gives the normal amount of saliva. By varying the length of intervals, one finds a specific time for each of the points. The negative effect of the fifth point, i. e., the absence of flow of saliva, was brought about by an internal inhibition, owing to the repetition of its stimulation without

the administration of food (this is also shown by the fact that before it became a negative factor it caused a flow of saliva, and only on repeated stimulation without food did it take on its negative properties). When this inhibitory activity is excited, it spreads at a certain speed to the other points, inhibiting them too. This is the mechanism of irradiation.

If the interval of time between the excitation of the fifth point and the one nearest to it is longer than was necessary to cause complete absence of flow of saliva on exciting the last one, one begins to have a gradual return to normal. This occurs similarly with the points further away, but the intervals of time have different proportions. This return to normal constitutes the mechanism of concentration. Both of these mechanisms are found also in the process of excitation. They may be expressed in the following law: "Any exciting or inhibiting process, started at some point in the cerebral hemispheres by virtue of definite peripheral stimulants, is subject to certain types of movements along the surface of the hemispheres, the rate of which can be measured not only by seconds, but also by minutes. These movements are in two directions: (1) spreading (irradiation); (2) return to original point (concentration)."

Chapters 17 to 21, inclusive, are taken up with a discussion of the pathologic conditions met with in the study of animal behavior. The chapters on the functional disturbances are preceded by a general discussion of the so-called "temperaments" or types of make-up and their relationship to the ease with which a disturbance in the dog's behavior occurs. The "sanguine" dog, e. g., forms new reflexes comparatively easily, but succumbs just as easily to particularly difficult situations with the development of what Pavlov considers an equivalent to mental disturbances in human beings. The "melancholic" dog, on the contrary, has greater difficulty in adapting itself to new situations, but shows more stability in face of adverse conditions.

In the chapters on the organic disturbances, Pavlov discusses the results of surgical operations on the cerebral cortex and the effect these have on the behavior of the animals.

With the rapidly growing interest manifested by physiologists, psychologists and neuropsychiatrists alike in the work on conditioned reflexes, a discussion of its importance in the study of human behavior is superfluous. It may be emphasized, however, that no presentation of this work, no matter how good, can come up to this remarkable book either in clearness or in completeness. The translation is masterly and shows both an intimate understanding of the original and an ability to present it in English.

HANDBUCH DER NEUROLOGIE. By O. BUMKE and O. FOERSTER. Volume 2, Parts 1, 2, 3 and 4. Price, 199 Rm. Pp. 1148, with 570 illustrations.

The second volume of the revision of Lewandowsky's Handbuch der Neurologie, the original of which appeared before the World War, consists of four separate volumes. While this edition is under the supervision of Professors O. Bumke and O. Foerster, all of four parts have been written by Professor Foerster. They comprise 1,148 pages with 570 illustrations, many of them in color. All the illustrations are excellent, and the color work is particularly fine.

The first part of the second volume deals with the special anatomy and physiology of the peripheral nerves; the second with the symptomatology of gunshot wounds of the peripheral nerves; the third with the therapy of gunshot injuries of the peripheral nerves, and the last with traumatic lesions of the spinal cord based on experiences gained in the World War.

The original Handbuch was unquestionably the best exposition of the German point of view regarding organic neurology at the time when it appeared. Many of the original authors are dead. The first part, which is divided into two volumes, appeared in 1922 and 1924. These have already been reviewed. The second volume of the Handbuch, which is here reviewed, lends itself particularly to revision, for knowledge of the anatomy, physiology and particularly the symptomatology and surgery of the peripheral nerves and of the spinal cord has been

so much enlarged by war experience that necessarily they must be rewritten in the light of these advances. There is no one on the continent of Europe today who could have done this work better than Professor Foerster, who is generally acknowledged to be the outstanding neurologist of Germany.

It would be impossible to review these volumes in detail. It is by far the best presentation of knowledge of the peripheral nerves and traumatic lesions of the spinal cord which has appeared since the World War.

DELINQUENCY AREAS. A STUDY OF THE GEOGRAPHIC DISTRIBUTION OF SCHOOL TRUANTS, JUVENILE DELINQUENTS, AND ADULT OFFENDERS IN CHICAGO. By CLIFFORD R. SHAW, with the collaboration of FREDERICK M. ZORBAUGH, HENRY D. MCKAY and LEONARD S. COTTRELL. Behavior Research Fund Monograph. Price, $4.00. Pp. 214. Chicago: University of Chicago Press, 1929.

If the second monograph from the Institute for Juvenile Research is a measure of the type of work that we are to expect, then the object for which this research has been founded will be more than fulfilled. Broadly speaking, the object of this research is investigation of behavior in human beings according to geographic distribution; it represents a study of delinquency from the point of view of its relation to the social situation in which it occurs. It is a study of the geographic distribution of school truants, juvenile delinquents and adult offenders in the city of Chicago. The work entailed in tabulating the material of this study has extended over a period of eight years and began in 1921. The study is based on statistics of approximately 60,000 school truants, juvenile delinquents and adult offenders.

The observations are of great import and show that there are marked variations between areas in Chicago in the rate of school truants, juvenile delinquents and adult offenders. Some are classified by very high rates while others show very low rates. These differences are seen in all the series studied. Secondly, the rate of such delinquency tends to vary inversely in proportion to the distance from the center of the city. In general, the nearer to the center of the city a given locality is, the higher will be its rate of delinquency and crime. Thirdly, there is a marked similarity in the distribution. Those communities which show the highest rates of juvenile delinquency also show, as a rule, the highest rates of truancy and adult crime. Fourthly, the difference of rates of truancy, delinquency and crime reflect differences in community backgrounds. High rates occur in the areas that are characterized by physical deterioration and declining population.

The interpretation of these observations is obvious.

DIE DYNAMIK DER BLUT ZIRKULATION IM GEHIRN. By E. SEPP. Monograph a. d. ges. Neurol. u. Psychiat., 53. Berlin: Julius Springer, 1928.

Sepp takes from the work of others certain anatomic observations, viz.: The first unique thing about the structure of brain vessels is the structure of the capillaries. Ranvier saw a double wall to brain capillaries, and Evensen proved the presence of a nonfenestrated elastic membrane in the capillaries of the brain. Sepp says that in Bielschowsky preparations a structureless membrane is visible, which folds in an irregular way when the wall of the artery shrinks. Over these lie many fibers going in different directions, which come from the "feet" of the glia about the vessel.

From the anatomic standpoint, these observations are doubtful. Is there any good evidence that the capillaries of the brain are different from those of other organs of the body? The fact that some observers state that Weigert's resorcin-fuchsin stain shows a fine dark line is not sure evidence of the presence of an impermeable elastic membrane. Moreover, no evidence is submitted to show that the capillaries of other organs do not also have this lamina elastica. Therefore, when the author goes on to build a special theory of cerebral circulation on this

evidence and states that, unlike capillaries elsewhere, those in the brain "cannot dilate — cannot transude fluid," he is probably building his whole theory on false premises. He says that transudation take place in the arterioles and resorption in the venules. The rest of the book is unjustifiable speculation on this basis.

One is surprised that such a manuscript could have been passed by the editors of this excellent monograph series.

THE MEASUREMENT OF NERVOUS HABITS IN NORMAL CHILDREN. By WILLARD C. OLSON. Price, $2. Pp. 94. Minneapolis: Univ. Minn. Press, 1929.

Some years ago, the University of Minnesota established a research department for the study of normal children chiefly from the psychologic standpoint. This research work is now beginning to bear fruit, and the book which is herein reviewed is an outstanding example of what can be expected from the study of normal persons, not only from the clinical but also from the psychologic standpoint.

The study has three general objectives: (1) the development of criteria of nervous habits in normal children; (2) the determination of the genesis and incidence of nervous habits in children, and (3) the development of differential tests and measures. After a preliminary study of technic and the evaluation of the reliability, constancy and validity of various nervous habits, observations were made on a certain number of children who had oral, nasal, hirsutal, ocular, aural and genital nervous habits. So far as sex is concerned, girls have in general a larger amount of nervous habits. An attempt was made to trace their genesis. The trend of evidence suggests that the causation is multiple. In general it may be said that family predisposition, association with persons of nervous habits, fatigue, habit formation and nutritional status are factors in the development of the habits studied.

From the neurologic standpoint this study is of the utmost importance, for it shows that normal children have certain habit formations and that not every child who is brought to a neurologist with such habits is necessarily a pathologic subject. The study of normal persons offers one of the most fertile fields for investigation.

THE CHILD OF CIRCUMSTANCE. THE MYSTERY OF THE UNBORN. By ALBERT WILSON, M.D. (Edinburgh). Price, $6.00. Pp. 420. New York: William Wood & Company, 1929.

This book is apparently for the layman. While the author states that this work covers the changes which have occurred in the last hundred years in the treatment for the constitutionally inferior, there is much that is not up to date, and none of it is new to the scientific man. It is undoubtedly enlightening to the average person, particularly so to those interested in prison reform or social service. While his definition of what crime is is not strictly speaking scientific, much might be learned from his sympathy and humane attitude toward the unfortunate mental cripple. The medical man will find much of it superficial and not always according to facts, at least, facts as they are today.

The interpretation of Freud is unique and certainly entirely original. Many physicians of greater scientific standing than Dr. Wilson, while not accepting all of Freud's theories without question, nevertheless have weighed and measured him with the fairness of an unprejudiced mind.

To an American the statement that any good we may have is due to British ancestry is too amusing to be taken seriously.

COMPARATIVE NEUROLOGY. A MANUAL AND TEXT FOR THE STUDY OF THE NERVOUS SYSTEM OF VERTEBRATES. By JAMES W. PAPEZ, B.A., M.D. Price, $6.00. Pp. 518, with 315 illustrations. New York: Thomas Y. Crowell Company, 1929.

Papez has written an excellent work on comparative neurology. The urge for the book grew out of the need of a laboratory course given in Cornell University, Ithaca, N. Y., to students of biology, physiology, psychology and those preparing

for the study of medical sciences. The book is divided into three parts. The first deals with the gross structure of the brain of mammals and discusses the entire nervous structure from the lower mammal to and including that of the cat, the dog and primates. In the second part the microscopic structure of the mammalian nervous system is discussed, and in the third the brains of lower vertebrates. The author has written the textbook largely on the basis of his own individual researches. The illustrations are excellent and really illustrate what the author is talking about. The method of presentation is good; the book is not too long, yet long enough. In every way the book fulfils the purpose of the author, and it is recommended particularly to all students of biology and psychology.

GENERAL PARALYSIS AND ITS TREATMENT BY INDUCED MALARIA. By E. T. MEAGHER. Price, 2 shillings. Pp. 88. London: His Majesty's Stationery Office, 1929.

The preface of this report contains a most interesting historical consideration of dementia paralytica from the earliest times until 1922 by Hubert Bond. The body of the report contains some interesting statistics. In England in 1923, there were 624 paretic patients admitted to hospitals for mental diseases, of which 90 per cent were dead and 8 per cent were living in the asylums in 1927. Of the 2 per cent, only two persons are able to work. In 1924, the fate of untreated patients was little better. After five years of malarial treatment of 1,597 patients only 33 per cent were dead, 40 per cent were in hospitals and 25 per cent were discharged. Even of those still remaining in hospitals about 36 per cent were improved while another third had not progressed. Other than these interesting statistics, this brochure contains no new information.

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